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Search Results - Record(s) 1 through 10 of 66 returned.

☐ 1. Document ID: US 20020039786 A1

L1: Entry 1 of 66 File: PGPB Apr 4, 2002

PGPUB-DOCUMENT-NUMBER: 20020039786
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020039786 A1

TITLE: Liver tissue source

PUBLICATION-DATE: April 4, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Reid, Lola M.	Chapel Hill	NC	US	
Lecluyse, Edward L.	Chapel Hill	NC	US	

US-CL-CURRENT: 435/325; 435/366, 435/372

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 2. Document ID: US 20020028497 A1

L1: Entry 2 of 66 File: PGPB Mar 7, 2002

PGPUB-DOCUMENT-NUMBER: 20020028497
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020028497 A1

TITLE: METHOD FOR PRODUCING RECOMBINANT ADENOVIRUS

PUBLICATION-DATE: March 7, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
BLANCHE, FRANCIS	PARIS		FR	
GUILLAUME, JEAN-MARC	PARIS		FR	

US-CL-CURRENT: 435/235.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 3. Document ID: US 20020028194 A1

L1: Entry 3 of 66 File: PGPB Mar 7, 2002

PGPUB-DOCUMENT-NUMBER: 20020028194
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020028194 A1

TITLE: Transgene expression systems

PUBLICATION-DATE: March 7, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Kaplan, Johanne	Sherborn	MA	US	
Armentano, Donna	Belmont	MA	US	
Gregory, Richard J.	Westford	MA	US	

US-CL-CURRENT: 424/93.21; 435/320.1, 435/456

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 4. Document ID: US 20020019051 A1

L1: Entry 4 of 66 File: PGPB Feb 14, 2002

PGPUB-DOCUMENT-NUMBER: 20020019051
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020019051 A1

TITLE: Chimeric adenoviral vectors

PUBLICATION-DATE: February 14, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Lusky, Monika	Freiburg		DE	
Winter, Arend Jan	Strasbourg		FR	

US-CL-CURRENT: 435/457; 435/235.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 5. Document ID: US 20020019002 A1

L1: Entry 5 of 66 File: PGPB Feb 14, 2002

PGPUB-DOCUMENT-NUMBER: 20020019002
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020019002 A1

TITLE: Methods of monitoring enzyme activity

PUBLICATION-DATE: February 14, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Griffiths, Gary	Oldham		GB	

US-CL-CURRENT: 435/6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 6. Document ID: US 20020009706 A1

L1: Entry 6 of 66 File: PGPB Jan 24, 2002

PGPUB-DOCUMENT-NUMBER: 20020009706
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020009706 A1

TITLE: Method for loading cells with an agent

PUBLICATION-DATE: January 24, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
McHale, Anthony P.	Portstewart		IE	
Craig, Roger K.	Cheshire		GB	
Fadlon, Emma	Portstewart		IE	

US-CL-CURRENT: 435/2; 435/810

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 7. Document ID: US 20020006902 A1

L1: Entry 7 of 66 File: PGPB Jan 17, 2002

PGPUB-DOCUMENT-NUMBER: 20020006902
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020006902 A1

TITLE: Combinations and methods for promoting in vivo liver cell proliferation and enhancing in vivo liver-directed gene transduction

PUBLICATION-DATE: January 17, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Alison, Malcolm R.	London	CA	GB	
Coutelle, Charles	London		GB	
Forbes, Stuart J.	London		GB	
Hodgson, Humphrey J.F.	London		GB	
Sarosi, Ildiko	Newbury Park		US	
Themis, Michael	Oxfordshire		GB	

US-CL-CURRENT: 514/12; 514/567

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 8. Document ID: US 20010053549 A1

L1: Entry 8 of 66 File: PGPB Dec 20, 2001

PGPUB-DOCUMENT-NUMBER: 20010053549
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010053549 A1

TITLE: Loading method

PUBLICATION-DATE: December 20, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
McHale, Anthony P.	Portstewart		GB	
Craig, Roger	Smallwood		GB	
Fadlon, Emma Jane	Portstewart		GB	

US-CL-CURRENT: 435/446; 435/173.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 9. Document ID: US 20010044651 A1

L1: Entry 9 of 66 File: PGPB Nov 22, 2001

PGPUB-DOCUMENT-NUMBER: 20010044651
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010044651 A1

TITLE: Expandable stent with sliding and locking radial elements

PUBLICATION-DATE: November 22, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Steinke, Thomas A.	San Diego	CA	US	
Koenig, Donald H.	San Diego	CA	US	

US-CL-CURRENT: 623/1.16; 623/1.17

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 10. Document ID: US 20010031497 A1

L1: Entry 10 of 66 File: PGPB Oct 18, 2001

PGPUB-DOCUMENT-NUMBER: 20010031497
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010031497 A1

TITLE: Chitosan related compositions and methods for delivery of nucleic acids and oligonucleotides into a cell

PUBLICATION-DATE: October 18, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Rolland, Alain	The Woodlands	TX	US	
Mumper, Russell J.	The Woodlands	TX	US	

US-CL-CURRENT: 435/455; 514/44, 536/20, 536/23.1

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Term	Documents
APO.DWPI,EPAB,JPAB,USPT,PGPB.	2940
APOES	0
APOS.DWPI,EPAB,JPAB,USPT,PGPB.	149
APOE.DWPI,EPAB,JPAB,USPT,PGPB.	501
A.DWPI,EPAB,JPAB,USPT,PGPB.	25713439
AS.DWPI,EPAB,JPAB,USPT,PGPB.	132941
APOLIPOPROTEIN$3	0
APOLIPOPROTEIN.DWPI,EPAB,JPAB,USPT,PGPB.	2066
APOLIPOPROTEINA.DWPI,EPAB,JPAB,USPT,PGPB.	3
APOLIPOPROTEINASE.DWPI,EPAB,JPAB,USPT,PGPB.	2
APOLIPOPROTEINA-I.DWPI,EPAB,JPAB,USPT,PGPB.	2
((APO(A) OR APOLIPOPROTEIN$3) SAME (ANTISENS$3 OR RIBOZYM$3)).USPT,PGPB,JPAB,EPAB,DWPI.	66

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Search Results - Record(s) 11 through 20 of 66 returned.

☐ 11. Document ID: US 20010016354 A1

L1: Entry 11 of 66 File: PGPB Aug 23, 2001

PGPUB-DOCUMENT-NUMBER: 20010016354
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010016354 A1

TITLE: Regulated expression of cloned genes using a cascade genetic circuit

PUBLICATION-DATE: August 23, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Cebolla Ramirez, Angel	Sevilla		ES	
Martin, Carolina Sousa	Sevilla		ES	
Prieto, Victor de Lorenzo	Sevilla		ES	

US-CL-CURRENT: 435/455; 435/320.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 12. Document ID: US 20010014476 A1

L1: Entry 12 of 66 File: PGPB Aug 16, 2001

PGPUB-DOCUMENT-NUMBER: 20010014476
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20010014476 A1

TITLE: CIRCULAR DNA MOLECULE WITH CONDITIONAL ORIGIN OF REPLICATION, METHOD FOR PREPARING THE SAME AND USE THEREOF IN GENE THERAPY

PUBLICATION-DATE: August 16, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
CROUZET, JOEL	SCEAUX		FR	
SOUBRIER, FABIENNE	THIAIS		FR	

US-CL-CURRENT: 435/455; 435/252.3, 435/252.33, 435/320.1, 435/325, 435/6, 435/91.4, 514/44, 536/23.1, 536/24.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 13. Document ID: US 20010008758 A1

L1: Entry 13 of 66 File: PGPB Jul 19, 2001

PGPUB-DOCUMENT-NUMBER: 20010008758
PGPUB-FILING-TYPE: new-utility
DOCUMENT-IDENTIFIER: US 20010008758 A1

TITLE: Delivery of an agent

PUBLICATION-DATE: July 19, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
McHale, Anthony Patrick	Portstewart		GB	
Craig, Roger	Sandbach Cheshire		GB	
Haro, Ana Maria Rollan	Londonberry		GB	

US-CL-CURRENT: 435/2; 424/93.7, 435/325

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 14. Document ID: US 6362198 B1

L1: Entry 14 of 66 File: USPT Mar 26, 2002

US-PAT-NO: 6362198
DOCUMENT-IDENTIFIER: US 6362198 B1

TITLE: Oxy substituted 4-carboxyamino-2-methyl-1,2,3,4-tetrahydroquinolines

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 15. Document ID: US 6358507 B1

L1: Entry 15 of 66 File: USPT Mar 19, 2002

US-PAT-NO: 6358507
DOCUMENT-IDENTIFIER: US 6358507 B1

TITLE: Transgene expression systems

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 16. Document ID: US 6344436 B1

L1: Entry 16 of 66 File: USPT Feb 5, 2002

US-PAT-NO: 6344436

DOCUMENT-IDENTIFIER: US 6344436 B1

TITLE: Lipophilic peptides for macromolecule delivery

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 17. Document ID: US 6322976 B1

L1: Entry 17 of 66 File: USPT Nov 27, 2001

US-PAT-NO: 6322976
DOCUMENT-IDENTIFIER: US 6322976 B1

TITLE: Compositions and methods of disease diagnosis and therapy

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 18. Document ID: US 6310075 B1

L1: Entry 18 of 66 File: USPT Oct 30, 2001

US-PAT-NO: 6310075
DOCUMENT-IDENTIFIER: US 6310075 B1

TITLE: Annulated 4-carboxyamino-2-methyl-1,2,3,4-tetrahydroquinolines

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 19. Document ID: US 6297010 B1

L1: Entry 19 of 66 File: USPT Oct 2, 2001

US-PAT-NO: 6297010
DOCUMENT-IDENTIFIER: US 6297010 B1

TITLE: Method for detecting and identifying mutations

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 20. Document ID: US 6248725 B1

L1: Entry 20 of 66 File: USPT Jun 19, 2001

US-PAT-NO: 6248725
DOCUMENT-IDENTIFIER: US 6248725 B1

TITLE: Combinations and methods for promoting in vivo liver cell proliferation and enhancing in vivo liver-directed gene transduction

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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Term	Documents
APO.DWPI,EPAB,JPAB,USPT,PGPB.	2940
APOES	0
APOS.DWPI,EPAB,JPAB,USPT,PGPB.	149
APOE.DWPI,EPAB,JPAB,USPT,PGPB.	501
A.DWPI,EPAB,JPAB,USPT,PGPB.	25713439
AS.DWPI,EPAB,JPAB,USPT,PGPB.	132941
APOLIPOPROTEIN$3	0
APOLIPOPROTEIN.DWPI,EPAB,JPAB,USPT,PGPB.	2066
APOLIPOPROTEINA.DWPI,EPAB,JPAB,USPT,PGPB.	3
APOLIPOPROTEINASE.DWPI,EPAB,JPAB,USPT,PGPB.	2
APOLIPOPROTEINA-I.DWPI,EPAB,JPAB,USPT,PGPB.	2
((APO(A) OR APOLIPOPROTEIN$3) SAME (ANTISENS$3 OR RIBOZYM$3)).USPT,PGPB,JPAB,EPAB,DWPI.	66

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Search Results - Record(s) 21 through 30 of 66 returned.

☐ 21. Document ID: US 6245512 B1

L1: Entry 21 of 66 File: USPT Jun 12, 2001

US-PAT-NO: 6245512
DOCUMENT-IDENTIFIER: US 6245512 B1

TITLE: Promoter for VEGF receptor

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 22. Document ID: US 6221849 B1

L1: Entry 22 of 66 File: USPT Apr 24, 2001

US-PAT-NO: 6221849
DOCUMENT-IDENTIFIER: US 6221849 B1

TITLE: DNA methyltransferase genomic sequences and antisense oligonucleotides

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 23. Document ID: US 6197786 B1

L1: Entry 23 of 66 File: USPT Mar 6, 2001

US-PAT-NO: 6197786
DOCUMENT-IDENTIFIER: US 6197786 B1

TITLE: 4-Carboxyamino-2-substituted-1,2,3,4-tetrahydroquinolines

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 24. Document ID: US 6184037 B1

L1: Entry 24 of 66 File: USPT Feb 6, 2001

US-PAT-NO: 6184037
DOCUMENT-IDENTIFIER: US 6184037 B1

TITLE: Chitosan related compositions and methods for delivery of nucleic acids and

oligonucleotides into a cell

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 25. Document ID: US 6177554 B1

L1: Entry 25 of 66 File: USPT Jan 23, 2001

US-PAT-NO: 6177554
DOCUMENT-IDENTIFIER: US 6177554 B1

TITLE: Nucleic acid transporter systems

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 26. Document ID: US 6177259 B1

L1: Entry 26 of 66 File: USPT Jan 23, 2001

US-PAT-NO: 6177259
DOCUMENT-IDENTIFIER: US 6177259 B1

TITLE: Assays and kits for inhibition of polyglutamine-induced cell death

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 27. Document ID: US 6150168 A

L1: Entry 27 of 66 File: USPT Nov 21, 2000

US-PAT-NO: 6150168
DOCUMENT-IDENTIFIER: US 6150168 A

TITLE: Nucleic acid transporter systems and methods of use

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 28. Document ID: US 6147090 A

L1: Entry 28 of 66 File: USPT Nov 14, 2000

US-PAT-NO: 6147090
DOCUMENT-IDENTIFIER: US 6147090 A

TITLE: 4-carboxyamino-2-methyl-1,2,3,4,-tetrahydroquinolines

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 29. Document ID: US 6147089 A

L1: Entry 29 of 66 File: USPT Nov 14, 2000

US-PAT-NO: 6147089
DOCUMENT-IDENTIFIER: US 6147089 A

TITLE: Annulated 4-carboxyamino-2-methyl-1,2,3,4,-tetrahydroquinolines

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 30. Document ID: US 6143727 A

L1: Entry 30 of 66 File: USPT Nov 7, 2000

US-PAT-NO: 6143727
DOCUMENT-IDENTIFIER: US 6143727 A

TITLE: Specific expression vectors and methods of use

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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Term	Documents
APO.DWPI,EPAB,JPAB,USPT,PGPB.	2940
APOES	0
APOS.DWPI,EPAB,JPAB,USPT,PGPB.	149
APOE.DWPI,EPAB,JPAB,USPT,PGPB.	501
A.DWPI,EPAB,JPAB,USPT,PGPB.	25713439
AS.DWPI,EPAB,JPAB,USPT,PGPB.	132941
APOLIPOPROTEIN$3	0
APOLIPOPROTEIN.DWPI,EPAB,JPAB,USPT,PGPB.	2066
APOLIPOPROTEINA.DWPI,EPAB,JPAB,USPT,PGPB.	3
APOLIPOPROTEINASE.DWPI,EPAB,JPAB,USPT,PGPB.	2
APOLIPOPROTEINA-I.DWPI,EPAB,JPAB,USPT,PGPB.	2
((APO(A) OR APOLIPOPROTEIN$3) SAME (ANTISENS$3 OR RIBOZYM$3)).USPT,PGPB,JPAB,EPAB,DWPI.	66

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Search Results - Record(s) 31 through 40 of 66 returned.

☐ 31. Document ID: US 6143530 A

L1: Entry 31 of 66 File: USPT Nov 7, 2000

US-PAT-NO: 6143530
DOCUMENT-IDENTIFIER: US 6143530 A

TITLE: Circular DNA expression cassettes for in vivo gene transfer

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 32. Document ID: US 6140343 A

L1: Entry 32 of 66 File: USPT Oct 31, 2000

US-PAT-NO: 6140343
DOCUMENT-IDENTIFIER: US 6140343 A

TITLE: 4-amino substituted-2-substituted-1,2,3,4-tetrahydroquinolines

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 33. Document ID: US 6140342 A

L1: Entry 33 of 66 File: USPT Oct 31, 2000

US-PAT-NO: 6140342
DOCUMENT-IDENTIFIER: US 6140342 A

TITLE: Oxy substituted 4-carboxyamino-2-methyl-1,2,3,4-tetrahydroquinolines

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 34. Document ID: US 6127175 A

L1: Entry 34 of 66 File: USPT Oct 3, 2000

US-PAT-NO: 6127175
DOCUMENT-IDENTIFIER: US 6127175 A

TITLE: Cells for the production of recombinant adenoviruses

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 35. Document ID: US 6103470 A

L1: Entry 35 of 66 File: USPT Aug 15, 2000

US-PAT-NO: 6103470
DOCUMENT-IDENTIFIER: US 6103470 A

TITLE: Plasmid for delivery of nucleic acids to cells and methods of use

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 36. Document ID: US 6100086 A

L1: Entry 36 of 66 File: USPT Aug 8, 2000

US-PAT-NO: 6100086
DOCUMENT-IDENTIFIER: US 6100086 A

TITLE: Transgene expression systems

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 37. Document ID: US 6043077 A

L1: Entry 37 of 66 File: USPT Mar 28, 2000

US-PAT-NO: 6043077
DOCUMENT-IDENTIFIER: US 6043077 A

TITLE: Hepatitis C virus ribozymes

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 38. Document ID: US 6033884 A

L1: Entry 38 of 66 File: USPT Mar 7, 2000

US-PAT-NO: 6033884
DOCUMENT-IDENTIFIER: US 6033884 A

TITLE: Nucleic acid transporter systems and methods of use

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 39. Document ID: US 5994109 A

L1: Entry 39 of 66 File: USPT Nov 30, 1999

US-PAT-NO: 5994109
DOCUMENT-IDENTIFIER: US 5994109 A

TITLE: Nucleic acid transporter system and methods of use

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 40. Document ID: US 5980886 A

L1: Entry 40 of 66 File: USPT Nov 9, 1999

US-PAT-NO: 5980886
DOCUMENT-IDENTIFIER: US 5980886 A

TITLE: Recombinant vectors for reconstitution of liver

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

Generate Collection | Print

Term	Documents
APO.DWPI,EPAB,JPAB,USPT,PGPB.	2940
APOES	0
APOS.DWPI,EPAB,JPAB,USPT,PGPB.	149
APOE.DWPI,EPAB,JPAB,USPT,PGPB.	501
A.DWPI,EPAB,JPAB,USPT,PGPB.	25713439
AS.DWPI,EPAB,JPAB,USPT,PGPB.	132941
APOLIPOPROTEIN$3	0
APOLIPOPROTEIN.DWPI,EPAB,JPAB,USPT,PGPB.	2066
APOLIPOPROTEINA.DWPI,EPAB,JPAB,USPT,PGPB.	3
APOLIPOPROTEINASE.DWPI,EPAB,JPAB,USPT,PGPB.	2
APOLIPOPROTEINA-I.DWPI,EPAB,JPAB,USPT,PGPB.	2
((APO(A) OR APOLIPOPROTEIN$3) SAME (ANTISENS$3 OR RIBOZYM$3)).USPT,PGPB,JPAB,EPAB,DWPI.	66

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Search Results - Record(s) 41 through 50 of 66 returned.

☐ 41. Document ID: US 5968502 A

L1: Entry 41 of 66 File: USPT Oct 19, 1999

US-PAT-NO: 5968502
DOCUMENT-IDENTIFIER: US 5968502 A

TITLE: Protein production and protein delivery

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 42. Document ID: US 5958764 A

L1: Entry 42 of 66 File: USPT Sep 28, 1999

US-PAT-NO: 5958764
DOCUMENT-IDENTIFIER: US 5958764 A

TITLE: Specific expression vectors and methods of use

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 43. Document ID: US 5958684 A

L1: Entry 43 of 66 File: USPT Sep 28, 1999

US-PAT-NO: 5958684
DOCUMENT-IDENTIFIER: US 5958684 A

TITLE: Diagnosis of neurodegenerative disease

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 44. Document ID: US 5916763 A

L1: Entry 44 of 66 File: USPT Jun 29, 1999

US-PAT-NO: 5916763
DOCUMENT-IDENTIFIER: US 5916763 A

TITLE: Promoter for VEGF receptor

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 45. Document ID: US 5914265 A

L1: Entry 45 of 66 File: USPT Jun 22, 1999

US-PAT-NO: 5914265
DOCUMENT-IDENTIFIER: US 5914265 A

TITLE: Keratin K1 expression vectors and methods of use

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 46. Document ID: US 5885968 A

L1: Entry 46 of 66 File: USPT Mar 23, 1999

US-PAT-NO: 5885968
DOCUMENT-IDENTIFIER: US 5885968 A

TITLE: Triantennary cluster glycosides, their preparation and use

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 47. Document ID: US 5877009 A

L1: Entry 47 of 66 File: USPT Mar 2, 1999

US-PAT-NO: 5877009
DOCUMENT-IDENTIFIER: US 5877009 A

TITLE: Isolated ApoA-I gene regulatory sequence elements

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 48. Document ID: US 5866551 A

L1: Entry 48 of 66 File: USPT Feb 2, 1999

US-PAT-NO: 5866551
DOCUMENT-IDENTIFIER: US 5866551 A

TITLE: Recombinant adero viruses comprising an inserted gene encoding apolipoprotein and their use in gene therapy for dyslipoproteinemias

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 49. Document ID: US 5856435 A

L1: Entry 49 of 66 File: USPT Jan 5, 1999

US-PAT-NO: 5856435
DOCUMENT-IDENTIFIER: US 5856435 A

TITLE: Nucleic acid-containing composition, its preparation and use

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 50. Document ID: US 5821235 A

L1: Entry 50 of 66 File: USPT Oct 13, 1998

US-PAT-NO: 5821235
DOCUMENT-IDENTIFIER: US 5821235 A

TITLE: Gene therapy using the intestine

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

Generate Collection | Print

Term	Documents
APO.DWPI,EPAB,JPAB,USPT,PGPB.	2940
APOES	0
APOS.DWPI,EPAB,JPAB,USPT,PGPB.	149
APOE.DWPI,EPAB,JPAB,USPT,PGPB.	501
A.DWPI,EPAB,JPAB,USPT,PGPB.	25713439
AS.DWPI,EPAB,JPAB,USPT,PGPB.	132941
APOLIPOPROTEIN$3	0
APOLIPOPROTEIN.DWPI,EPAB,JPAB,USPT,PGPB.	2066
APOLIPOPROTEINA.DWPI,EPAB,JPAB,USPT,PGPB.	3
APOLIPOPROTEINASE.DWPI,EPAB,JPAB,USPT,PGPB.	2
APOLIPOPROTEINA-I.DWPI,EPAB,JPAB,USPT,PGPB.	2
((APO(A) OR APOLIPOPROTEIN$3) SAME (ANTISENS$3 OR RIBOZYM$3)).USPT,PGPB,JPAB,EPAB,DWPI.	66

There are more results than shown above. Click here to view the entire set.

Display Format: - Change Format

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Generate Collection | Print

Search Results - Record(s) 51 through 60 of 66 returned.

☐ 51. Document ID: US 5786340 A

L1: Entry 51 of 66 File: USPT Jul 28, 1998

US-PAT-NO: 5786340
DOCUMENT-IDENTIFIER: US 5786340 A

TITLE: Gene transfer to the intestine

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 52. Document ID: US 5763270 A

L1: Entry 52 of 66 File: USPT Jun 9, 1998

US-PAT-NO: 5763270
DOCUMENT-IDENTIFIER: US 5763270 A

TITLE: Plasmid for delivery of nucleic acids to cells and methods of use

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 53. Document ID: US 5747340 A

L1: Entry 53 of 66 File: USPT May 5, 1998

US-PAT-NO: 5747340
DOCUMENT-IDENTIFIER: US 5747340 A

TITLE: Targeted gene expression using preproendothelin-1 promoters

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 54. Document ID: US 5733761 A

L1: Entry 54 of 66 File: USPT Mar 31, 1998

US-PAT-NO: 5733761
DOCUMENT-IDENTIFIER: US 5733761 A

TITLE: Protein production and protein delivery

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 55. Document ID: US 5721138 A

L1: Entry 55 of 66 File: USPT Feb 24, 1998

US-PAT-NO: 5721138
DOCUMENT-IDENTIFIER: US 5721138 A

TITLE: Apolipoprotein(A) promoter and regulatory sequence constructs and methods of use

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 56. Document ID: US 5705388 A

L1: Entry 56 of 66 File: USPT Jan 6, 1998

US-PAT-NO: 5705388
DOCUMENT-IDENTIFIER: US 5705388 A

TITLE: CETP Ribozymes

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 57. Document ID: US 5695977 A

L1: Entry 57 of 66 File: USPT Dec 9, 1997

US-PAT-NO: 5695977
DOCUMENT-IDENTIFIER: US 5695977 A

TITLE: Site directed recombination

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 58. Document ID: WO 200112789 A2, AU 200069101 A

L1: Entry 58 of 66 File: DWPI Feb 22, 2001

DERWENT-ACC-NO: 2001-202860
DERWENT-WEEK: 200120
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TITLE: New apolipoprotein B mRNA-specific ribozyme, useful for treating diseases characterized by excessive plasma levels of apolipoprotein B, e.g. atherosclerosis, hypercholesterolemia or hyperlipidemia

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 59. Document ID: AU 200068259 A, WO 200107066 A2

L1: Entry 59 of 66 File: DWPI Feb 13, 2001

DERWENT-ACC-NO: 2001-159640
DERWENT-WEEK: 200128

TITLE: Use of inhibitors of Peroxisome Proliferator Activated Receptor delta, for preventing foam cell development from macrophages or other cells or removing foam cells for treating e.g. vascular diseases

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 60. Document ID: US 2001016354 A1, WO 200078976 A1, AU 200054172 A

L1: Entry 60 of 66 File: DWPI Aug 23, 2001

DERWENT-ACC-NO: 2001-102726
DERWENT-WEEK: 200151

TITLE: Cascade genetic circuit useful for regulated expression of cloned genes, comprises several nucleic acid constructs encoding regulators arranged in order and final target promoter responsive in dose-dependent fashion

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

Generate Collection | Print

Term	Documents
APO.DWPI,EPAB,JPAB,USPT,PGPB.	2940
APOES	0
APOS.DWPI,EPAB,JPAB,USPT,PGPB.	149
APOE.DWPI,EPAB,JPAB,USPT,PGPB.	501
A.DWPI,EPAB,JPAB,USPT,PGPB.	25713439
AS.DWPI,EPAB,JPAB,USPT,PGPB.	132941
APOLIPOPROTEIN$3	0
APOLIPOPROTEIN.DWPI,EPAB,JPAB,USPT,PGPB.	2066
APOLIPOPROTEINA.DWPI,EPAB,JPAB,USPT,PGPB.	3
APOLIPOPROTEINASE.DWPI,EPAB,JPAB,USPT,PGPB.	2
((APO(A) OR APOLIPOPROTEIN$3) SAME (ANTISENS$3 OR RIBOZYM$3)).USPT,PGPB,JPAB,EPAB,DWPI.	66

There are more results than shown above. Click here to view the entire set.

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Search Results - Record(s) 61 through 66 of 66 returned.

☐ 61. Document ID: EP 1165143 A2, WO 200057920 A2, AU 200035682 A

L1: Entry 61 of 66 File: DWPI Jan 2, 2002

DERWENT-ACC-NO: 2000-647208
DERWENT-WEEK: 200209

TITLE: Regulating expression of transgenes encoding enzymes or hormones in mammals, by transforming expandable population of cells with desired transgene and regulating cell proliferation by administration of an agent

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 62. Document ID: BR 200009333 A, WO 200057837 A2, AU 200039187 A, EP 1171078 A2, NO 200104657 A

L1: Entry 62 of 66 File: DWPI Jan 8, 2002

DERWENT-ACC-NO: 2000-647196
DERWENT-WEEK: 200208

TITLE: Modulating levels of high density, low density and very low density lipoprotein cholesterol and apolipoprotein AI, using LIPG genes or polypeptides and modulators of their expression and activity

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 63. Document ID: EP 1108051 A2, FR 2782732 A1, WO 200012741 A2, AU 9954262 A

L1: Entry 63 of 66 File: DWPI Jun 20, 2001

DERWENT-ACC-NO: 2000-285227
DERWENT-WEEK: 200135

TITLE: Inducible expression system useful for gene therapy comprises a transcriptional activator cassette and a recombinant adenoviral vector containing a transactivatable promoter

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

☐ 64. Document ID: MX 9904449 A1, WO 9822607 A1, FR 2756297 A1, ZA 9710516 A, AU 9852261 A, NO 9902464 A, CZ 9901822 A3, EP 946741 A1, SK 9900666 A3, BR 9713388 A, HU 200001762 A2, AU 731106 B, JP 2001503993 W, KR 2000057202 A

L1: Entry 64 of 66 File: DWPI Feb 1, 2000

DERWENT-ACC-NO: 1998-312491
DERWENT-WEEK: 200123

TITLE: Production of defective recombinant virus using baculovirus for complementation - used for cloning genes and for in vivo or in vitro expression of genes, e.g. as nucleic acid vaccines

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

☐ 65. Document ID: KR 2000053163 A, WO 9821349 A1, FR 2755699 A1, ZA 9710114 A, AU 9850578 A, NO 9902153 A, CZ 9901633 A3, EP 946740 A1, SK 9900614 A3, HU 9904235 A2, BR 9713981 A, MX 9904019 A1, JP 2001503279 W

L1: Entry 65 of 66 File: DWPI Aug 25, 2000

DERWENT-ACC-NO: 1998-297952
DERWENT-WEEK: 200121

TITLE: New vectors and variant promoters for inducible, liver-specific expression - are derived from the human apolipoprotein AII promoter and are useful for gene therapy

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Image

☐ 66. Document ID: US 2001014476 A1, WO 9710343 A1, FR 2738842 A1, AU 9669924 A, ZA 9607640 A, NO 9801044 A, CZ 9800788 A3, EP 850310 A1, SK 9800347 A3, BR 9610511 A, HU 9900018 A2, MX 9802005 A1, JP 2000501281 W, KR 99044683 A, AU 728231 B

L1: Entry 66 of 66 File: DWPI Aug 16, 2001

DERWENT-ACC-NO: 1997-202239
DERWENT-WEEK: 200149

TITLE: Recombinant plasmid with conditional origin of replication - can replicate at high copy number only in presence of specific foreign protein, useful for gene therapy and production of recombinant proteins

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw. Desc | Clip Img | Image

Generate Collection | Print

Term	Documents
APO.DWPI,EPAB,JPAB,USPT,PGPB.	2940
APOES	0
APOS.DWPI,EPAB,JPAB,USPT,PGPB.	149
APOE.DWPI,EPAB,JPAB,USPT,PGPB.	501
A.DWPI,EPAB,JPAB,USPT,PGPB.	25713439
AS.DWPI,EPAB,JPAB,USPT,PGPB.	132941
APOLIPOPROTEIN$3	0
APOLIPOPROTEIN.DWPI,EPAB,JPAB,USPT,PGPB.	2066
APOLIPOPROTEINA.DWPI,EPAB,JPAB,USPT,PGPB.	3
APOLIPOPROTEINASE.DWPI,EPAB,JPAB,USPT,PGPB.	2
((APO(A) OR APOLIPOPROTEIN$3) SAME (ANTISENS$3 OR RIBOZYM$3)).USPT,PGPB,JPAB,EPAB,DWPI.	66

There are more results than shown above. Click here to view the entire set.

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? s ?lipoprotein? and (antisens? or ribozym?)
>>>File 155 processing for ?LIPOPROTEIN? stopped at ALPHAPRODINE
   --CHEMISTRY --CH
>>>File 5 processing for ?LIPOPROTEIN? stopped at ACTIVATORY
             2  ?LIPOPROTEIN?
         32890  ANTISENS?
          5717  RIBOZYM?
      S1    0  ?LIPOPROTEIN? AND (ANTISENS? OR RIBOZYM?)
? s lipoprotein? and (antisens? or ribozym?)
        149116  LIPOPROTEIN?
         32890  ANTISENS?
          5717  RIBOZYM?
      S2   216  LIPOPROTEIN? AND (ANTISENS? OR RIBOZYM?)
? s apoliporotein or apo (w) a
Processing
            20  APOLIPOROTEIN
         33818  APO
      13076038  A
          6668  APO(W)A
      S3  6684  APOLIPOROTEIN OR APO (W) A
? s s3 and (antisens? or ribozym?)
          6684  S3
         32890  ANTISENS?
          5717  RIBOZYM?
      S4    13  S3 AND (ANTISENS? OR RIBOZYM?)
? rd
...completed examining records
      S5     8  RD (unique items)
? t s5/3,ab/all

 5/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11334330   21214790   PMID: 11313820
   Adenovirus-mediated apo(a)-antisense -RNA expression
efficiently inhibits apo(a) synthesis in vitro and in vivo.
  Frank S; Gauster M; Strauss J; Hrzenjak A; Kostner GM
  Institute of Medical Biochemistry and Medical Molecular Biology,
Karl-Franzens-University Graz, Harrachgasse 21, 3rd Floor, 8010 Graz,
Austria.
  Gene therapy (England)  Mar 2001, 8 (6) p425-30, ISSN 0969-7128
Journal Code: CCE
  Languages: ENGLISH
  Document type: Journal Article
  Record type: Completed
  Apo(a ) is a very atherogenic plasma protein without apparent
function, which is highly expressed in humans. The variation in plasma
Lp(a) concentration among individuals is considerable. Approximately 10-15%
of the white population exhibit plasma Lp(a) concentrations above the
atherogenic cut-off value of approximately 30 mg/dl. Since there is
currently no safe way of treating those patients with drugs, we have tested
the possibility of interfering with apo(a) biosynthesis by
adenovirus-mediated expression of antisense apo(a) mRNA
comprising the 5' UTR, the signal sequence and the first three kringles of
native apo(a ). Transduction of rat hepatoma McA RH 7777 cells
which stably expressed apo(a) with 18 kringle IV (KIV) domains
with apo(a)-antisense adenovirus (AS-Ad) at multiplicity
of infection (MOI) of 30 reduced apo(a) synthesis to 23% as
compared with control cells. As apo(a) is not synthesized in
laboratory animals, we induced biosynthesis of the N-terminal fragments of
apo(a ) in mice by adenovirus-mediated gene transfer.
Cotransduction of these mice with AS-Ad, which expressed up to eight times
higher amounts of apo(a) than stable transgenic apo(
```

not human

a) mice, led to an almost complete disappearance of **apo(a**) from plasma. We conclude that the proposed AS-construct is very efficient in interfering with **apo(a)** biosynthesis in vivo. The strategy of inducing the synthesis of a nonexpressed protein followed by knocking it out by AS technology may also be applicable to other systems.

5/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10755310 99016008 PMID: 9799211
Novel therapeutic strategy for atherosclerosis: **ribozyme** oligonucleotides against apolipoprotein(a) selectively inhibit apolipoprotein(a) but not plasminogen gene expression.
Morishita R; Yamada S; Yamamoto K; Tomita N; Kida I; Sakurabayashi I; Kikuchi A; Kaneda Y; Lawn R; Higaki J; Ogihara T
Department of Geriatric Medicine, Osaka University Medical School Osaka, Japan.
Circulation (UNITED STATES) Nov 3 1998, 98 (18) p1898-904, ISSN 0009-7322 Journal Code: DAW
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
BACKGROUND: Because mechanisms of atherosclerosis by lipoprotein(a) [Lp(a)] have been postulated in the decrease in active transforming growth factor-beta conversion by decreased plasmin, selective decrease in apolipoprotein(a) [**apo(a)**] independent of plasminogen may have therapeutic values. Although **antisense** can decrease **apo(a**), its application may be difficult because of very high homology of **apo(a)** gene to plasminogen. Thus we used **ribozyme** strategy that actively cleaves targeted genes to selectively inhibit **apo(a)** expression. METHODS AND RESULTS: We constructed **ribozyme** oligonucleotides containing phosphorothioate DNA- and RNA-targeted kringle 4 of the **apo(a**) gene that showed 80% homology to plasminogen. Transfection of human **apo(a)** gene produced Lp(a) in medium of HepG2 cells, whereas Lp(a) could not be detected in control cells. Cotransfection of **ribozyme** and **apo(** **a)** gene resulted in the decrease in mRNA of **apo(a)** but not plasminogen. Moreover, marked decrease in Lp(a) was also observed in the medium transfected with **ribozyme** and **apo(a)** gene compared with **apo(a)** gene alone (P<0.01), whereas there was no significant change in plasminogen level between **ribozyme**-transfected and control cells. Incubation of human vascular smooth muscle cells (VSMC) with conditioned medium from **apo(a)**-transfected HepG2 cells resulted in a significant increase in VSMC number, whereas addition of conditioned medium from cells cotransfected with **ribozyme** oligonucleotides and **apo(a**) gene resulted in no VSMC growth (P<0.01). DNA-based control oligonucleotides and mismatched **ribozyme** oligonucleotides did not have an inhibitory effect on Lp(a) production. CONCLUSIONS: Overall, our data revealed that transfection of **ribozyme** against the **apo(a)** gene resulted in the selective inhibition of the **apo(a**) but not the plasminogen gene, providing novel therapeutic strategy for treatment of high Lp(a), a risk factor for atherosclerosis.

5/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10707156 20402319 PMID: 10942748
CC chemokine I-309 is the principal monocyte chemoattractant induced by apolipoprotein(a) in human vascular endothelial cells.
Haque NS; Zhang X; French DL; Li J; Poon M; Fallon JT; Gabel BR; Taubman MB; Koschinsky M; Harpel PC

Division of Hematology, Department of Medicine, Mount Sinai School of Medicine, New York, NY 10029, USA.
Circulation (UNITED STATES) Aug 15 2000, 102 (7) p786-92, ISSN 0009-7322 Journal Code: DAW
Contract/Grant No.: HL54469, HL, NHLBI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
BACKGROUND: Lipoprotein(a) [Lp(a)] is a risk factor for atherosclerosis; however, the mechanisms are unclear. We previously reported that Lp(a) stimulated human vascular endothelial cells to produce monocyte chemotactic activity. The apolipoprotein(a) [**apo**(**a**)] portion of Lp(a) was the active moiety. METHODS AND RESULTS: We now describe the identification of the chemotactic activity as being due to the CC chemokine I-309. The carboxy-terminal domain of **apo**(**a**) containing 6 type-4 kringles (types 5 to 10), kringle V, and the protease domain was demonstrated to contain the I-309-inducing portion. Polyclonal and monoclonal anti-I-309 antibodies as well as an antibody against a portion of the extracellular domain of CCR8, the I-309 receptor, inhibited the increase in monocyte chemotactic activity induced by **apo**(**a**). I-309 **antisense** oligonucleotides also inhibited the induction of endothelial monocyte chemotactic activity by **apo**(**a**). I-309 mRNA was identified in human umbilical vein endothelial cells. **Apo**(**a**) induced an increase in I-309 protein in the endothelial cytoplasm and in the conditioned medium. Immunohistochemical studies have identified I-309 in endothelium, macrophages, and extracellular areas of human atherosclerotic plaques and have found that I-309 colocalized with **apo**(**a**). CONCLUSIONS: These data establish that I-309 is responsible for the monocyte chemotactic activity induced in human umbilical vein endothelial cells by Lp(a). The identification of the endothelial cell as a source for I-309 suggests that this chemokine may participate in vessel wall biology. Our data also suggest that I-309 may play a role in mediating the effects of Lp(a) in atherosclerosis.

5/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10417537 20000485 PMID: 10532685
Secretion of prebeta HDL increases with the suppression of cholesteryl ester transfer protein in Hep G2 cells.
Sawada S; Sugano M; Makino N; Okamoto H; Tsuchida K
Department of Bioclimatology and Medicine, Medical Institute of Bioregulation, Kyushu University, Beppu, Oita, Japan.
Atherosclerosis (IRELAND) Oct 1999, 146 (2) p291-8, ISSN 0021-9150 Journal Code: 95X
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Prebeta HDL are small, protein rich lipoproteins that are predominantly composed of **apo A**-I, without **apo A**-II. Prebeta HDL are secreted from the liver as nascent HDL and/or are produced in the incubated plasma by cholesteryl ester transfer protein (CETP). However, the role of CETP in the secretion of HDL from the liver has yet to be determined. In the present study, we examined the effect of the suppression of hepatic CETP by **antisense** oligodeoxynucleotides (ODNs) against CETP targeted to the liver on the secretion of **apo A**-I using a Hep G2 cell culture. The ODNs against CETP were coupled to asialoglycoprotein (ASOR) carrier molecules, which serve as an important method for the regulation of liver gene expression. Hep G2 cells were cultured in DMEM supplemented with 10 FBS. After 2 days, the medium was changed to DMEM with EGF and the cells were divided into three groups. The control group received saline, while the sense group was mixed with the sense ODNs complex and the **antisense** group was mixed with the

antisense ODNs complex, respectively, for 2 days. Both the hepatic CETP mRNA and the CETP mass in the medium in the **antisense** group decreased significantly more than in the sense and the control groups (CETP mass: 1.697 + /- 0.410 ng/mg cell protein vs. 2.367 + /- 0.22 and 2.360 + /- 0.139, n = 3 in each determination). In contrast, both the hepatic **apo A**-I mRNA and the **apo A**-I mass in the medium in the **antisense** group were significantly higher than those in the sense and the control groups (**apo A**-I mass; 1.877 + /- 0.215 micro/mg cell protein vs. 1.213 + /- 0.282 and 1.097 + /- 0.144, n = 3 in each determination). The increase in **apo A**-I was mainly due to the increase in prebeta **apo A**-I. These findings may partly explain why HDL and **apo A**-I increase in patients with CETP deficiency, while also indicating the possibility that the original level of prebeta HDL is sufficient in such patients.

5/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06805175 92126396 PMID: 1772697
mRNA quantitation by a simple and sensitive RNAse protection assay.
Pape ME; Melchior GW; Marotti KR
Upjohn Company, Kalamazoo, Michigan 49001.
Genetic analysis, techniques and applications (UNITED STATES) Nov 1991, 8 (7) p206-13, ISSN 1050-3862 Journal Code: AP4
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

An RNAse protection assay is described that increases substantially the degree of precision with which one can measure the mRNA levels in cells and tissues through the use of the internal standard. The assay can be used to measure any mRNA for which the corresponding cDNA is available. We describe here the use of the assay to measure the apolipoprotein (**apo**)-**A**-I, apo-B, and apo-E mRNA levels in tissues from the cynomolgus monkey. cDNA fragments derived from each mRNA were subcloned into pGEM-9Zf(-), a vector containing a polylinker that is flanked by the SP6 and T7 RNA polymerase promoters. That series of plasmids, called RNA quantitation vectors (pRQV-AI, B, or E), permitted the synthesis of a sense RNA strand and an **antisense** RNA strand for the gene of interest. The sense stand was used as the internal standard and added to the RNA to be analyzed just prior to initiation of the assay. The radiolabeled **antisense** strand served as the probe. By including some nucleotides derived from the vector, we were able to design both the internal standard and the probe such that, after solution hybridization and RNAse digestion, the size of the protected internal standard-probe fragments was different from that of the authentic mRNA-probe fragments. Those fragments were then separated by gel electrophoresis, and the radioactivity in the authentic mRNA band was compared to that in the internal standard band. The mass of the authentic mRNA could then be calculated from the ratio of the radioactivity in each band and the mass of the internal standard.

5/3,AB/6 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13432296 BIOSIS NO.: 200200061117
Ribozymes targeted to **apo(A)** mRNA
AUTHOR: Stinchcomb D T; McSwiggen J; Newton R S; Ramharack R
AUTHOR ADDRESS: 7203 Old Post Rd., Boulder, Colo. 80301**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1195 (1):p377 Feb. 4, 1997
ISSN: 0098-1133
DOCUMENT TYPE: Patent

RECORD TYPE: Citation
LANGUAGE: English
1997

5/3,AB/7 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2002 BIOSIS. All rts. reserv.

11899113 BIOSIS NO.: 199900145222
Ribozymes targeted to **apo**(**a**) RNA.
AUTHOR: Stinchcomb D T; McSwiggen J; Newton R S; Ramharack R
AUTHOR ADDRESS: Boulder, Colo.**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents 1220 (1):p493 March 2, 1999
ISSN: 0098-1133
RECORD TYPE: Citation
LANGUAGE: English
1999

5/3,AB/8 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2002 BIOSIS. All rts. reserv.

10680330 BIOSIS NO.: 199799301475
Targeted delivery of **apo**(**a**)-specific **antisense** oligonucleotides to the hepatocyte.
AUTHOR: Biessen Erik A L; Vietsch Helene; Rump Erik T; Fluiter Kees; Van Berkel Theo J C
AUTHOR ADDRESS: Div. Biopharm., Leiden**Netherlands
JOURNAL: Circulation 94 (8 SUPPL.):pI39 1996
CONFERENCE/MEETING: 69th Scientific Sessions of the American Heart Association New Orleans, Louisiana, USA November 10-13, 1996
ISSN: 0009-7322
RECORD TYPE: Citation
LANGUAGE: English
1996
? ds

Set	Items	Description
S1	0	?LIPOPROTEIN? AND (ANTISENS? OR RIBOZYM?)
S2	216	LIPOPROTEIN? AND (ANTISENS? OR RIBOZYM?)
S3	6684	APOLIPOROTEIN OR APO (W) A
S4	13	S3 AND (ANTISENS? OR RIBOZYM?)
S5	8	RD (unique items)

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? s s2 not s4
             216  S2
              13  S4
      S6     209  S2 NOT S4
? rd
...examined 50 records  (50)
...examined 50 records  (100)
...examined 50 records  (150)
...examined 50 records  (200)
...completed examining records
      S7     140  RD (unique items)
? s s7 and apo?
>>>File 155 processing for APO? stopped at APOSTLES
>>>File 5 processing for APO? stopped at APOPHENYLETHYLAMINE
             140  S7
          213034  APO?
      S8      38  S7 AND APO?
? rd
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...completed examining records
S9 38 RD (unique items)
? t s9/3,ab/all

9/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12922028 21645927 PMID: 11786298
Stably transfected ABCA1 **antisense** cell line has decreased ABCA1 mRNA and cAMP-induced cholesterol efflux to **apolipoprotein** AI and HDL.
Zheng P; Horwitz A; Waelde C A; Smith J D
The Rockefeller University, 1230 York Avenue, New York, NY 10021, USA.
Biochimica et biophysica acta (Netherlands) Dec 30 2001, 1534 (2-3) p121-8, ISSN 0006-3002 Journal Code: 0217513
Contract/Grant No.: P01 HL54591, HL, NHLBI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Using a sensitive real time fluorescent PCR assay, ABCA1 mRNA levels were induced by approximately 50-70-fold following 8Br-cAMP treatment of the RAW264 murine macrophage cell line, concomitant with the induction of cholesterol efflux to **apoAI** and HDL. A stably transfected ABCA1 **antisense** cDNA cell line was created, which led to approximately 50-70% reductions in ABCA1 mRNA levels in basal and 8Br-cAMP-treated cells, and diminished to the same extent the 8Br-cAMP-mediated efflux of cholesterol to **apolipoprotein** AI and HDL. These data demonstrate that ABCA1 is necessary for the cAMP-induced lipid efflux to both **apoAI** and HDL.

9/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12903318 21683593 PMID: 11739389
Low density **lipoprotein** receptor-related protein mediates **apolipoprotein** E inhibition of smooth muscle cell migration.
Swertfeger Debi K; Bu Guojun; Hui David Y
Center for Lipid and Arteriosclerosis Studies, Department of Pathology and Laboratory Medicine, University of Cincinnati College of Medicine, Cincinnati, Ohio 45267, USA.
Journal of biological chemistry (United States) Feb 8 2002, 277 (6) p4141-6, ISSN 0021-9258 Journal Code: 2985121R
Contract/Grant No.: HL59150, HL, NHLBI; HL61332, HL, NHLBI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
This research was undertaken to identify the cell surface receptor responsible for mediating **apolipoprotein** E (**apoE**) inhibition of platelet-derived growth factor (PDGF)-directed smooth muscle cell migration. Initial studies revealed the expression of the low density **lipoprotein** receptor (LDLR), the LDL receptor-related protein (LRP), the very low density **lipoprotein** receptor (VLDL), and **apoE** receptor-2 in mouse aortic smooth muscle cells. Smooth muscle cells isolated from LDLR-null, VLDL-null, and **apoE** receptor-2-null mice were responsive to **apoE** inhibition of PDGF-directed smooth muscle cell migration, suggesting that these receptors were not involved. An **antisense** RNA expression knockdown strategy, utilizing morpholino **antisense** RNA against LRP, was used to reduce LRP expression in smooth muscle cells to assess the role of this receptor in **apoE** inhibition of cell migration. Results showed that **apoE** was unable to inhibit PDGF-directed migration of LRP-deficient smooth muscle cells. The role of LRP in mediating **apoE** inhibition of PDGF-directed smooth muscle cell migration was confirmed by experiments showing that antibodies

against LRP effectively suppressed **apoE** inhibition of PDGF-directed smooth muscle cell migration. Taken together, these results document that **apoE** binding to LRP is required for its inhibition of PDGF-directed smooth muscle cell migration.

9/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12839371 21587497 PMID: 11730811
Apolipoprotein AI and HDL(3) inhibit spreading of primary human monocytes through a mechanism that involves cholesterol depletion and regulation of CDC42.
Diederich W; Orso E; Drobnik W; Schmitz G
Institute of Clinical Chemistry and Laboratory Medicine, University of Regensburg, Franz-Josef-Strauss-Allee 11, D-93042, Regensburg, Germany.
Atherosclerosis (Ireland) Dec 2001, 159 (2) p313-24, ISSN 0021-9150 Journal Code: 0242543
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The objective of the current study was to characterize the influence of high density **lipoproteins** (HDL) on processes related to the vascular recruitment of human monocytes, which may contribute to the anti-atherogenic properties of these **lipoproteins** . We show that HDL(3) and **apo** AI inhibit the following processes in primary human monocytes: (1) M-CSF induced cell spreading; (2) M-CSF stimulated expression of surface molecules involved in adhesion, migration, and scavenging; (3) fMLP induced chemotaxis. These processes are obviously modulated by the regulation of cellular cholesterol pools as indicated by the following findings. In Tangier monocytes with defective **apo** AI induced cholesterol efflux, **apo** AI had no influence on the spreading response. In control cells, stimulation of cholesterol efflux by p-cyclodextrin mimicked the effect of **apo** AI and HDL(3) on spreading and chemotaxis, whereas cholesterol loading with enzymatically modified LDL (E-LDL) showed the opposite effect. Finally, a similar inverse regulation by E-LDL and **apo** AI/HDL(3) was also observed in regard to the surface expression of beta(1)- and beta(2)-integrins as well as the hemoglobin/haptoglobin scavenger receptor CD163 and the Fcgamma-IIIaR CD16. CDC42 was identified as a potential downstream target linking changes in cellular cholesterol content to monocyte spreading and chemotaxis. Thus, CDC42 **antisense** markedly reduced spreading and, in parallel with their influence on monocyte spreading, HDL(3), **apo** AI and p-cyclodextrin down-regulated CDC42 expression while E-LDL had the inverse effect. The **apo** AI induced decrease of CDC42 protein expression was paralleled by the reduction of active GTP-bound CDC42. In summary, we provide evidence that HDL(3) and **apo** AI are able to inhibit processes in primary human monocytes, which are related to the recruitment of monocytes into the vessel wall and probably involve regulation of cellular cholesterol pools and CDC42 function.

9/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12794708 21623612 PMID: 11604390
The low density **lipoprotein** receptor-related protein contributes to selective uptake of high density **lipoprotein** cholesteryl esters by SW872 liposarcoma cells and primary human adipocytes.
Vassiliou G; Benoist F; Lau P; Kavaslar G N; McPherson R
Lipoprotein and Atherosclerosis Group, University of Ottawa Heart Institute, Ottawa, Ontario K1Y 4E9, Canada. gvass@ottawaheart.ca
Journal of biological chemistry (United States) Dec 28 2001, 276 (52) p48823-30, ISSN 0021-9258 Journal Code: 2985121R

Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The concept that selective transfer of high density **lipoprotein** (HDL)-derived cholesteryl esters (CE) does not require **lipoprotein** internalization has been challenged recently by evidence that implicates HDL recycling during the selective uptake process. This has prompted us to examine the role of the low density **lipoprotein** receptor-related protein (LRP) in selective uptake. LRP is an endocytic receptor for **lipoprotein** lipase (LpL) and **apolipoprotein** E (**apoE**) ligands that are able to mediate selective uptake. We report that molecules that interfere with ligand binding to LRP, such as the receptor-associated protein (RAP), suramin, alpha(2)-macroglobulin, or lactoferrin, inhibit HDL-CE selective uptake by human primary adipocytes and SW872 liposarcoma cells by 35-50%. This partial inhibition of selective uptake from total HDL was not due to preferential inhibition of the HDL(2) or HDL(3) subfractions. Selective uptake by the scavenger receptor BI was not inhibited by RAP, excluding its involvement. Furthermore, in SW872 cells in which LRP was reduced to 14% of control levels by stable **antisense** expression, selective uptake was attenuated by at least 33%, confirming a role for LRP in this process. RAP, alpha(2)-macroglobulin, lactoferrin, and suramin (individually or in paired combinations) also attenuated selective uptake of HDL-CE by primary human adipocytes by about 40%. On the other hand, human skin fibroblasts express LRP abundantly but lack the capacity for selective uptake, demonstrating that other molecules are required. In SW872 cells, exogenous **apoE** or LpL can facilitate selective uptake but only the **apoE** -enhanced uptake can be inhibited by RAP, implicating **apoE** as a likely co-mediator. We discuss the possible mechanisms by which the endocytic receptor, LRP, can mediate selective uptake.

9/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12518521 21343344 PMID: 11451387
Estrogen increases hepatic lipase levels in inbred strains of mice: a possible mechanism for estrogen-dependent lowering of high density **lipoprotein**.
Srivastava N; Chowdhury P R; Averna M; Srivastava R A
Department of Internal Medicine, Washington University, St. Louis, MO, USA.
Molecular and cellular biochemistry (Netherlands) Apr 2001, 220 (1-2) p87-93, ISSN 0300-8177 Journal Code: 0364456
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We have shown mouse to be an useful animal model for studies on the estrogen-mediated synthesis and secretion of **lipoproteins** since, unlike in rats, low density **lipoprotein** receptors are not upregulated in mice. This results into the elevation of plasma levels of **apolipoprotein** (**apo**) B and **apoE**, and lowering of **apoA**-1-containing particles. The mechanisms of **apoB** and **apoE** elevation by estrogen have been elucidated, but the mechanism of lowering of plasma levels of HDL is still not known. Among other factors, **apoA**-I, cholesterol ester transfer protein (CETP), scavenger receptor B1 (SR-B1), and hepatic lipase are potential candidates that modulate plasma levels of HDL. Since estrogen treatment increased hepatic **apoA** -I mRNA and **apoA**-I synthesis, and mouse express undetectable levels of CETP, we tested the hypothesis that estradiol-mediated lowering of HDL in mice may occur through modulation of hepatic lipase (HL). Four mouse strains (C57L, C57BL, BALB, C3H) were administered supraphysiological doses of estradiol, and plasma levels of HDL as well as HL mRNA were quantitated. In all 4 strains estradiol decreased plasma levels of HDL by 30%, and

increased HL mRNA 2-3 fold. In a separate experiment groups of male C57BL mouse were castrated or sham-operated, and low and high doses of estradiol administered. We found 1.4-2.5 fold elevation of HL mRNA with concomitant lowering of HDL levels. Ten other mouse strains examined also showed estradiol-induced elevation of HL mRNA, but the extent of elevation was found to be strain-specific. Based on these studies, we conclude that hepatic lipase is an important determinant of plasma levels of HDL and that HL mRNA is modulated by estrogen which in turn may participate in the lowering of plasma levels of HDL.

9/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12501003 20549046 PMID: 11096445
Hammerhead **ribozyme** as a therapeutic agent for hyperlipidemia: production of truncated **apolipoprotein** B and hypolipidemic effects in a dyslipidemia murine model.
Enjoji M; Wang F; Nakamuta M; Chan L; Teng B B
Departments of Medicine and Cell Biology, Baylor College of Medicine, Houston, TX 77030, USA.
Human gene therapy (UNITED STATES) Nov 20 2000, 11 (17) p2415-30, ISSN 1043-0342 Journal Code: 9008950
Contract/Grant No.: HL51586, HL, NHLBI; HL53441, HL, NHLBI; HL59314, HL, NHLBI
Languages: ENGLISH
Document type: Journal Article
Record type: In Process
In humans, overproduction of **apolipoprotein** B (**apoB**) is positively associated with premature coronary artery diseases. To reduce the levels of **apoB** mRNA, we used adenovirus-mediated vector to target hammerhead **ribozyme** at GUA(6679) downward arrow of **apoB** mRNA (designated AvRB15) in the liver of a dyslipidemic mouse model that is deficient in **apoB** mRNA editing enzyme and overexpresses human **apoB100** . In this study, we delivered approximately 4 x 10(11) virus particles of AvRB15 (active **ribozyme**) or AvRB15-mutant (inactive **ribozyme**) to the animals. Using Southern blot analysis, we readily detected RB15 DNA in the mouse liver as long as day 35 after injection. This result was correlated with the RNA expression of RB15 by RNase protection assay. Using reverse ligation-mediated polymerase chain reaction, the 3' cleavage product of **apoB** mRNA was detected, and the exact cleavage site was confirmed by sequencing. Importantly, the levels of human and mouse **apoB** mRNA decreased approximately 80% after AvRB15 transduction. There was a marked decrease in plasma cholesterol, triglyceride, and human **apoB** of 42, 51, and 62%, respectively, when compared with the inactive **ribozyme**-treated group. Moreover, **ribozyme** cleavage of **apoB** mRNA generated a truncated protein of the expected size (**apoB48**.1), which was associated with **lipoprotein** particles in the very low density, low density, and high density **lipoprotein** fractions. Taken together, these results indicate that **apoB** mRNA-specific hammerhead **ribozyme** can be used as a potential therapeutic agent to modulate **apoB** gene expression and to treat hyperlipidemia.

9/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11178177 21105634 PMID: 11168996
Dual effect of oxidized LDL on cell cycle in human endothelial cells through oxidative stress.
Galle J; Heinloth A; Wanner C; Heermeier K
Division of Nephrology, Department of Medicine, University Hospital of Wurzburg, Wurzburg, Germany. j-c.galle@mail.uni-wuerzburg.de

Kidney international (United States) Feb 2001, 59 Suppl 78 pS120-3, ISSN 0085-2538 Journal Code: KVB
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
BACKGROUND: Oxidized low-density **lipoprotein** (OxLDL) exerts proliferation and **apoptosis** in vascular cells, depending on its concentration and the exposure time. Various steps in the cell cycle and in the **apoptotic** signaling cascade are modulated by O2-, and OxLDL stimulates vascular O2- formation. Here we studied the role of NADPH oxidase, a potential source for O2- formation after OxLDL stimulation, in cell proliferation, and we investigated whether OxLDL influences anti-**apoptotic** genes in cultured human umbilical vein endothelial cells (HUVEC). Methods and Results. OxLDL dose-dependently (10 to 300 microg/mL) stimulated O2- formation in HUVEC (detected by cytochrome c assay and by chemiluminescence of lucigenin). Low OxLDL concentrations (5 to 10 microg/mL) induced proliferation (detected by 3H-thymidine incorporation), while higher concentrations (50 to 300 microg/mL) induced **apoptotic** cell death (detected by Annexin assay and DNA fragmentation). Proliferation was blocked by the antioxidants SOD and catalase and by diphenyleneiodonium (10 micromol/L), an inhibitor of the O2- generating NADPH oxidase. In addition, cells transfected with **antisense** oligonucleotides for NADPH oxidase showed a significantly reduced O2- formation after stimulation with OxLDL. The OxLDL effect on **apoptosis** was also blocked by antioxidants. Since endothelial cells are protected against **apoptosis** through anti-**apoptotic** genes, we investigated whether OxLDL overcomes protection against **apoptosis** through suppression of the anti-**apoptotic** gene A20, a zinc-finger protein. OxLDL suppressed the expression of A20 in a dose-dependent manner. CONCLUSION: These data indicate that OxLDL has a dual effect on cell cycle in HUVEC, inducing proliferation at low and **apoptosis** at higher concentrations. Both effects are mediated by O2- formation, with NADPH oxidase being a major source for O2-. Thus, OxLDL contributes importantly to vascular cellular turnover through the induction of oxidative stress.

9/3,AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11152036 21093726 PMID: 11181793
Oxidized LDL suppresses NF-kappaB and overcomes protection from **apoptosis** in activated endothelial cells.
Heermeier K; Leicht W; Palmetshofer A; Ullrich M; Wanner C; Galle J
University Hospital, Department of Medicine, Division of Nephrology, University of Wurzburg, Wurzburg, Germany.
Journal of the American Society of Nephrology (United States) Mar 2001, 12 (3) p456-63, ISSN 1046-6673 Journal Code: A6H
Languages: ENGLISH
Document type: Journal Article
Record type: In Process
Atherosclerosis is a chronic inflammatory disease associated with enhanced **apoptotic** cell death in vascular cells, partly induced by oxidized low-density **lipoprotein** (OxLDL). However, proinflammatory stimuli such as lipopolysaccharide (LPS) or tumor necrosis factor-alpha (TNF-alpha) activate endothelial cells (EC) and inhibit **apoptosis** through induction of nuclear factor kappaB (NF-kappaB)-dependent genes. This study therefore investigated whether OxLDL or its component, lysophosphatidylcholine (LPC), interacts with the effect of LPS or TNF-alpha on cell survival. Human EC were incubated with LPS, TNF-alpha, OxLDL, or LPC alone or in combinations. OxLDL (100 to 200 microg/ml) and LPC (100 to 300 microM) induced **apoptosis** dose-dependently. LPS and TNF-alpha had no effect on cell survival in the presence or absence of OxLDL or LPC. LPS and TNF-alpha both induced the antiapoptotic gene A20, whereas OxLDL and LPC suppressed its induction. Expression of A20 is

regulated by NF-kappaB. OxLDL and LPC dose-dependently suppressed NF-kappaB activity. For functional analysis, bovine EC were transfected with A20 encoding expression constructs in sense and **antisense** orientation. Bovine EC that overexpressed A20 were protected against OxLDL-induced **apoptosis**, whereas expression of **antisense** A20 rendered cells more sensitive to OxLDL. These results suggest that OxLDL not only induces cell death, as has been shown before, but also compromises antiapoptotic protection of activated EC. OxLDL sensitizes EC to **apoptotic** triggers by interfering with the induction of A20 during the inflammatory response seen in atherosclerotic lesions. This inhibition is based on repression of NF-kappaB activation. The effect may be caused by the OxLDL component LPC.

9/3,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10968816 20562833 PMID: 11108728
Involvement of caveolin-1 in cholesterol enrichment of high density **lipoprotein** during its assembly by **apolipoprotein** and THP-1 cells.
Arakawa R; Abe-Dohmae S; Asai M; Ito JI; Yokoyama S
Biochemistry 1, Nagoya City University Medical School, Kawasumi 1, Mizuho-cho, Mizuho-ku, Nagoya 467-8601, Japan.
Journal of lipid research (UNITED STATES) Dec 2000, 41 (12) p1952-62 , ISSN 0022-2275 Journal Code: IX3
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
High density **lipoprotein** (HDL) is assembled by interaction of **apolipoprotein** A-I with human monocytic leukemia cell line THP-1 by removing cellular cholesterol and phospholipid. Although the HDL formed with undifferentiated THP-1 cells contained only phosphatidylcholine and almost no cholesterol, the cells differentiated with phorbol 12-myristate 13-acetate (PMA) generated HDL enriched in cholesterol. The extent of cholesterol enrichment related to the cellular cholesterol level in the differentiated cells, but only weakly in the undifferentiated cells. In contrast, the differentiation had no influence on the diffusion-mediated cellular cholesterol efflux. The undifferentiated cells expressed the messages of ATP-binding cassette transporter 1 and caveolin-1, at low levels, and the PMA-induced differentiation resulted in substantial expression of both messages. Caveolin-1 protein expression was also highly induced by the PMA treatment of THP-1 cells. When the cells were treated with the **antisense** DNA of caveolin-1 and differentiated, both caveolin-1 synthesis and cholesterol incorporation into the HDL were reduced in parallel to generate the cholesterol-poor HDL.We concluded that caveolin-1 is involved in enrichment with cholesterol of the HDL generated by the **apolipoprotein**-cell interaction. This function is independent of the assembly of HDL particles with cellular phospholipid and of nonspecific, diffusion-mediated efflux of cellular cholesterol.

9/3,AB/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10958205 20524378 PMID: 11069947
Neuronal **apoptosis** by **apolipoprotein** E4 through low-density **lipoprotein** receptor-related protein and heterotrimeric GTPases.
Hashimoto Y; Jiang H; Niikura T; Ito Y; Hagiwara A; Umezawa K; Abe Y; Murayama Y; Nishimoto I
Department of Pharmacology and Neurosciences, KEIO University School of Medicine, Shinanomachi, Tokyo 160, Japan.
journal of neuroscience (UNITED STATES) Nov 15 2000, 20 (22) p8401-9 , ISSN 1529-2401 Journal Code: DOO
Languages: ENGLISH

Document type: Journal Article
Record type: Completed
The epsilon4 genotype of **apolipoprotein** E (**apoE4**) is the most established predisposing factor in Alzheimer's disease (AD); however, it remains unclear how **apoE4** contributes to the pathophysiology. Here, we report that the **apoE4** protein (**ApoE4**) evokes **apoptosis** in neuronal cells through the low-density **lipoprotein** receptor-related protein (LRP) and heterotrimeric GTPases. We examined neuron/neuroblastoma hybrid F11 cells and found that these cells were killed by 30 microg/ml **ApoE4**, but not by 30 microg/ml **ApoE3**. **ApoE4**-induced death occurred with typical features for **apoptosis** in time- and dose-dependent manners, and was observed in SH-SY5Y neuroblastomas, but not in glioblastomas or non-neuronal Chinese hamster ovary cells. Activated, but not native, alpha2-macroglobulin suppressed this **ApoE4** toxicity. Suppression by the **antisense** oligonucleotide to LRP and inhibition by low nanomolar concentrations of LRP-associated protein RAP provided evidence for the involvement of LRP. The involvement of heterotrimeric GTPases was demonstrated by the findings that (1) **ApoE4**-induced death was suppressed by pertussis toxin (PTX), but not by heat-inactivated PTX; and (2) transfection with PTX-resistant mutant cDNAs of Galpha(i) restored the toxicity of **ApoE4** restricted by PTX. We thus conclude that one of the neurotoxic mechanisms triggered by **ApoE4** is to activate a cell type-specific **apoptogenic** program involving LRP and the G(i) class of GTPases and that the **apoE4** gene may play a direct role in the pathogenesis of AD and other forms of dementia.

9/3,AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10951495 20573604 PMID: 11123936
Low- and high-density **lipoprotein** metabolism in HepG2 cells expressing various levels of **apolipoprotein** E.
Charpentier D; Tremblay C; Rassart E; Rhainds D; Auger A; Milne RW; Brissette L
Departement des Sciences Biologiques, Universite du Quebec a Montreal, C.P. 8888, Succ. Centre-ville, Montreal, Quebec, Canada.
Biochemistry (UNITED STATES) Dec 26 2000, 39 (51) p16084-91, ISSN 0006-2960 Journal Code: A0G
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
To determine the importance of hepatic **apolipoprotein** (**apo**) E in **lipoprotein** metabolism, HepG2 cells were transfected with a constitutive expression vector (pRc/CMV) containing either the complete or the first 474 base pairs of the human **apoE** cDNA inserted in an **antisense** orientation, for **apoE** gene inactivation, or the full-length human **apoE** cDNA inserted in a sense orientation for overexpression of **apoE** . Stable transformants were obtained that expressed 15, 24, 226, and 287% the **apoE** level of control HepG2 cells. The metabolism of low-density **lipoprotein** (LDL) and high-density **lipoprotein**-3 (HDL(3)), two **lipoprotein** classes following both holoparticle and cholesteryl esters (CE)-selective uptake pathways, was compared between all these cells. LDL-protein degradation, an indicator of the holoparticle uptake, was greater in low **apoE** expressing cells than in control or high expressing cells, while HDL(3)-protein degradation paralleled the **apoE** levels of the cells (r(2) = 0.989). LDL- and HDL(3)-protein association was higher in low **apoE** expressing cells compared to control cells. In opposition, LDL- and HDL(3)-CE association was not different from control cells in low **apoE** expressing cells but rose in high **apoE** expressing cells. In consequence, the CE-selective uptake (CE/protein association ratio) was positively correlated with the level of **apoE** expression in all cells

for both LDL (r(2) = 0.977) and HDL(3) (r(2) = 0.998). We also show that, although in normal and low **apoE** expressor cells, 92% of LDL- and 80% HDL(3)-CE hydrolysis is sensitive to chloroquine suggesting a pathway linked to lysosomes for both **lipoproteins**, cells overexpressing **apoE** lost 60% of chloroquine-sensitive HDL(3)-CE hydrolysis without affecting that of LDL-CE. Thus, the level of **apoE** expression in HepG2 cells determines the fate of LDL and HDL(3).

9/3,AB/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10934630 20576309 PMID: 10995777
SMAD proteins transactivate the human **ApoCIII** promoter by interacting physically and functionally with hepatocyte nuclear factor 4.
Kardassis D; Pardali K; Zannis VI
Department of Basic Sciences, University of Crete Medical School and Institute of Molecular Biology and Biotechnology, F.O.R.T.H., Heraklion GR-71110, Crete, Greece.
Journal of biological chemistry (UNITED STATES) Dec 29 2000, 275 (52) p41405-14, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: HL33952, HL, NHLBI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Cotransfection of HepG2 cells with SMADs established that SMAD3 and SMAD3-SMAD4 transactivated (15-70-fold) the -890/+24 **apoCIII** promoter and shorter promoter segments, whereas cotransfection with a dominant negative SMAD4 mutant repressed the **apoCIII** promoter activity by 50%, suggesting that SMAD proteins participate in **apoCIII** gene regulation. Transactivation required the presence of a hormone response element, despite the fact that SMADs could not bind directly to it. Cotransfection of SMAD3-SMAD4 along with hepatocyte nuclear factor-4 resulted in a strong synergistic transactivation of the -890/+24 **apoCIII** promoter, proximal promoter segments, or synthetic promoters containing either the **apoCIII** enhancer or the proximal **apoCIII** hormone response element. Inhibition of endogenous hepatocyte nuclear factor-4 synthesis by an **antisense ribozyme** construct reduced the constitutive activity of the **apoCIII** promoter in HepG2 cells to 10% and abolished the SMAD-mediated transactivation. Co-immunoprecipitation and GST pull-down assays provided evidence for physical interactions between SMAD3, SMAD4, and hepatic nuclear factor-4. Our findings indicate that transforming growth factor beta and its signal transducer SMAD proteins can modulate gene transcription by novel mechanisms that involve their physical and functional interaction with hepatocyte nuclear factor-4, suggesting that SMAD proteins may play an important role in **apolipoprotein** gene expression and **lipoprotein** metabolism.

9/3,AB/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10894426 20549005 PMID: 11095961
Neuronal cell **apoptosis** by a receptor-binding domain peptide of **ApoE4**, not through low-density **lipoprotein** receptor-related protein.
Hagiwara A; Hashimoto Y; Niikura T; Ito Y; Terashita K; Kita Y; Nishimoto I; Umezawa K
Department of Applied Chemistry, Keio University, Yokohama, Japan.
Biochemical and biophysical research communications (UNITED STATES) Nov 30 2000, 278 (3) p633-9, ISSN 0006-291X Journal Code: 9Y8
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Since an **apolipoprotein** E4 (**ApoE4**) peptide composed of the low-density **lipoprotein** (LDL) receptor-related protein (LRP)-binding domain [**ApoE4**(141-149)(2) or **ApoE** (141-155)(2)] exerts neurotoxicity in primary neurons and neuronal cell lines, it has been controversial whether these effects are mediated by LRP. Here, we examined whether **ApoE4** (141-149)(2)-induced toxicity is mediated by LRP in a neuronal cell system where **ApoE4** toxicity is mediated by LRP: serum-deprived F11 neuronal cells. In these cells, where **ApoE4** exerted toxicity by **apoptosis** in a manner sensitive to both caspase inhibitors and pertussis toxin (PTX), **ApoE4**(141-149)(2) also caused cell death by **apoptosis** but in a caspase-inhibitor-resistant, PTX-resistant manner. **ApoE4** (141-149)(2)-induced death was not inhibited by **antisense** oligonucleotides to LRP. Therefore, we conclude that **ApoE4** (141-149)(2) is able to exert neurotoxicity without involving LRP. Copyright 2000 Academic Press.

9/3,AB/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10857349 20432356 PMID: 10974057
Normal high density **lipoprotein** inhibits three steps in the formation of mildly oxidized low density **lipoprotein**: steps 2 and 3.
Navab M; Hama SY; Anantharamaiah GM; Hassan K; Hough GP; Watson AD; Reddy ST; Sevanian A; Fonarow GC; Fogelman AM
Atherosclerosis Research Unit, Division of Cardiology, Department of Medicine, University of California, Los Angeles, Los Angeles, CA 90095, USA.
Journal of lipid research (UNITED STATES) Sep 2000, 41 (9) p1495-508, ISSN 0022-2275 Journal Code: IX3
Contract/Grant No.: HL 30568, HL, NHLBI; HL 34343, HL, NHLBI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Treatment of human artery wall cells with **apolipoprotein** A-I (**apoA**-I), but not **apoA**-II, with an **apoA**-I peptide mimetic, or with high density **lipoprotein** (HDL), or paraoxonase, rendered the cells unable to oxidize low density **lipoprotein** (LDL). Human aortic wall cells were found to contain 12-lipoxygenase (12-LO) protein. Transfection of the cells with **antisense** to 12-LO (but not sense) eliminated the 12-LO protein and prevented LDL-induced monocyte chemotactic activity. Addition of 13(S)-hydroperoxyoctadecadienoic acid [13(S)-HPODE] and 15(S)-hydroperoxyeicosatetraenoic acid [15(S)-HPETE] dramatically enhanced the nonenzymatic oxidation of both 1-palmitoyl-2-arachidonoyl-sn-glycero-3-phosphocholine (PAPC) and cholesteryl linoleate. On a molar basis 13(S)-HPODE and 15(S)-HPETE were approximately two orders of magnitude greater in potency than hydrogen peroxide in causing the formation of biologically active oxidized phospholipids (m/z 594, 610, and 828) from PAPC. Purified paraoxonase inhibited the biologic activity of these oxidized phospholipids. HDL from 10 of 10 normolipidemic patients with coronary artery disease, who were neither diabetic nor receiving hypolipidemic medications, failed to inhibit LDL oxidation by artery wall cells and failed to inhibit the biologic activity of oxidized PAPC, whereas HDL from 10 of 10 age- and sex-matched control subjects did.We conclude that a) mildly oxidized LDL is formed in three steps, one of which involves 12-LO and each of which can be inhibited by normal HDL, and b) HDL from at least some coronary artery disease patients with normal blood lipid levels is defective both in its ability to prevent LDL oxidation by artery wall cells and in its ability to inhibit the biologic activity of oxidized PAPC.

9/3,AB/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10819590 20461022 PMID: 11004212
Stimulation of NADPH oxidase by oxidized low-density **lipoprotein** induces proliferation of human vascular endothelial cells.
Heinloth A; Heermeier K; Raff U; Wanner C; Galle J
Department of Medicine, Division of Nephrology, University Hospital of Wurzburg, Wurzburg, Germany.
Journal of the American Society of Nephrology (UNITED STATES) Oct 2000, 11 (10) p1819-25, ISSN 1046-6673 Journal Code: A6H
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Oxidized low-density **lipoprotein** (OxLDL) exerts proliferation and **apoptosis** in vascular cells, depending on its concentration and the duration of exposure. Recent studies indicate that [O(2)](-) is involved in cell cycle regulation and that OxLDL stimulates endothelial cells to produce [O(2)](-). This study examined the role of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase as a potential source for [O(2)](-) in the proliferation-inducing activity of OxLDL in cultured human umbilical vein endothelial cells (HUVEC). Human LDL was oxidized by Cu(++), and proliferation of HUVEC was detected by 3H-thymidine incorporation. OxLDL (5 microg/ml) caused an increase in proliferation of HUVEC of 250 to 300%. OxLDL-induced proliferation was blocked by addition of the antioxidants superoxide dismutase and catalase, suggesting that enhanced [O(2)](-) formation was involved. Diphenylene iodonium (DPI, 1 microM), an inhibitor of NADPH oxidase, also prevented OxLDL-induced proliferation of HUVEC, indicating that NADPH oxidase was the source for enhanced [O(2)](-) formation. The OxLDL effect was mimicked by lysophosphatidylcholine (LPC, 10 microM), a compound formed during oxidation of LDL. LPC-induced proliferation was also prevented by coincubation with DPI. Treatment of HUVEC with [O(2)](-) generated by the xanthine/xanthine oxidase reaction resulted in proliferation as did treatment with OxLDL. As expected, this stimulation could not be blocked by DPI. With the use of the cytochrome c-assay, it was demonstrated that OxLDL and LPC enhanced [O(2)](-) formation in HUVEC (by factor 3.2 and by factor 3.5, respectively). Supporting the assumption that NADPH oxidase was the enzyme responsible for [O(2)](-) formation, cells transfected with **antisense** oligonucleotides for NADPH oxidase showed a significantly reduced [O(2)](-) formation after stimulation with OxLDL and LPC. OxLDL and its compound LPC induce proliferation of HUVEC through activation of NADPH oxidase. The active NADPH oxidase generates [O(2)](-), which mediates the proliferative effects.

9/3,AB/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10745669 98148046 PMID: 9478952
Effect of **antisense** oligonucleotides against cholesteryl ester transfer protein on the development of atherosclerosis in cholesterol-fed rabbits.
Sugano M; Makino N; Sawada S; Otsuka S; Watanabe M; Okamoto H; Kamada M; Mizushima A
Department of Bioclimatology and Medicine, Medical Institute of Bioregulation, Kyushu University, 4546 Tsurumihara, Beppu, Oita 874, Japan.
Journal of biological chemistry (UNITED STATES) Feb 27 1998, 273 (9) p5033-6, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Cholesteryl ester transfer protein (CETP) is the enzyme that facilitates the transfer of cholesteryl ester from high density **lipoprotein** (HDL) to **apolipoprotein** B (**apoB**)-containing **lipoproteins** . However, the exact role of CETP in the development of atherosclerosis has not been determined. In the present study, we examined the effect of the

suppression of increased plasma CETP by intravenous injection with **antisense** oligodeoxynucleotides (ODNs) against CETP targeted to the liver on the development of atherosclerosis in rabbits fed a cholesterol diet. The ODNs against rabbit CETP were coupled to asialoglycoprotein (ASOR) carrier molecules, which serve as an important method to regulate liver gene expression. Twenty-two male Japanese White rabbits were used in the experiment. Eighteen animals were fed a standard rabbit chow supplemented with 0.3% cholesterol throughout the experiment for 16 weeks. At 8 weeks, they were divided into three groups (six animals in each group), among which the plasma total and HDL cholesterol concentrations did not significantly change. The control group received nothing, the sense group were injected with the sense ODNs complex, and the **antisense** group were injected with the **antisense** ODNs complex, respectively, for subsequent 8 weeks. ASOR. poly(L-lysine) ODNs complex were injected via the ear veins twice a week. Four animals were fed a standard rabbit diet for 16 weeks. The total cholesterol concentrations and the CETP mass in the animals injected with **antisense** ODNs were all significantly decreased in 12 and 16 weeks compared with those injected with sense ODNs and the control animals. The HDL cholesterol concentrations measured by the precipitation assay did not significantly change among the groups fed a cholesterol diet, and triglyceride concentrations did not significantly change in the four groups. However, at the end of the study, when the HDL cholesterol concentrations were measured after the isolation by ultracentrifugation and a column chromotography, they were significantly higher in the animals injected with **antisense** ODNs than in the animals injected with sense ODNs and in the control animals. A reduction of CETP mRNA and an increase of LDL receptor mRNA in the liver were observed in the animals injected with **antisense** ODNs compared with those injected with sense ODNs and the control animals. Aortic cholesterol contents and the aortic percentage lesion to total surface area were significantly lower in the animals injected with **antisense** ODNs than in the animals injected with sense ODNs and in the control animals. These findings showed for the first time that suppression of increased plasma CETP by the injection with **antisense** ODNs against CETP coupled to ASOR carrier molecules targeted to the liver could thus inhibit the atherosclerosis possibly by decreasing the plasma LDL + very low density **lipoprotein** (VLDL) cholesterol in cholesterol-fed rabbits.

9/3,AB/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10716382 20387407 PMID: 10827200

The assembly of very low density **lipoproteins** in rat hepatoma McA-RH7777 cells is inhibited by phospholipase A2 antagonists.

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Journal of biological chemistry (UNITED STATES) Aug 11 2000, 275 (32) p25023-30, ISSN 0021-9258 Journal Code: HIV

Contract/Grant No.: CA09422, CA, NCI; CA85757, CA, NCI

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

In McA-RH7777 cells, the oleate-stimulated assembly and secretion of very low density **lipoproteins** (VLDL) was associated with enhanced deacylation of phospholipids, which was markedly decreased by inactivation of the cellular phospholipase A(2). Treatment of the cells with antagonists or **antisense** oligonucleotide of the Ca(2+)-independent phospholipase A(2) (iPLA(2)) significantly inhibited secretion of **apoB100**-VLDL and triglyceride. Similar inhibitory effect of the iPLA(2) antagonists was observed on **apoB48**-VLDL secretion, but secretion of high density **lipoprotein** particles (such as **apoAI**- and **apoB48**-high

density **lipoprotein**) or proteins in general was unaffected. The iPLA(2) antagonist did not affect the synthesis of **apoB100** or triglyceride, nor did it affect the activities of phospholipase D, phosphatidate phosphohydrolase, or microsomal triglyceride transfer protein. Inactivation of iPLA(2) resulted in impaired **apoB100**-VLDL assembly as shown by decreased **apoB100**-VLDL and triglyceride within the microsomal lumen, with concomitant increase in **apoB100** association with the microsomal membranes. The inhibitory effect of iPLA(2) antagonists on **apoB100** -VLDL assembly/secretion could be abated by pretreatment of cells with oleate. Analysis of molecular species of microsomal phosphatidylcholine and phosphatidylethanolamine by electron spray tandem mass spectrometry revealed that the enrichment of oleoyl moieties was altered by the treatment of iPLA(2) antagonist. These results suggest that the oleate-induced VLDL assembly/secretion may depend upon the establishment of membrane glycerolipids enriched in oleoyl chain, a process mediated by the iPLA(2) activity.

9/3,AB/18 (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10574753 20229804 PMID: 10766831
Megalin acts in concert with cubilin to mediate endocytosis of high density **lipoproteins**.
Hammad SM; Barth JL; Knaak C; Argraves WS
Department of Cell Biology and Anatomy, Medical University of South Carolina, Charleston, South Carolina 29425-2204, USA.
Journal of biological chemistry (UNITED STATES) Apr 21 2000, 275 (16) p12003-8, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: HL07710, HL, NHLBI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Cubilin has recently been shown to function as an endocytic receptor for high density **lipoproteins** (HDL). The lack of apparent transmembrane and cytoplasmic domains in cubilin raises questions as to the means by which it can mediate endocytosis. Since cubilin has been reported to bind the endocytic receptor megalin, we explored the possibility that megalin acts in conjunction with cubilin to mediate HDL endocytosis. While megalin did not bind to HDL, delipidated HDL, or **apoA**-I, it was found to copurify with cubilin isolated by HDL-Sepharose affinity chromatography. Cubilin and megalin exhibited coincident patterns of mRNA expression in mouse tissues including the kidney, ileum, thymus, placenta, and yolk sac endoderm. The expression of both receptors in yolk sac endoderm-like cells was inducible by retinoic acid treatment but not by conditions of sterol depletion. Suppression of megalin activity or expression by treatment with either megalin antibodies or megalin **antisense** oligodeoxynucleotides resulted in inhibition of cubilin-mediated endocytosis of HDL. Furthermore, megalin **antisense** oligodeoxynucleotide treatment resulted in reduced cell surface expression of cubilin. These data demonstrate that megalin acts together with cubilin to mediate HDL endocytosis and further suggest that megalin may play a role in the intracellular trafficking of cubilin.

9/3,AB/19 (Item 19 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10555077 20230197 PMID: 10764682
Upregulation of endothelial receptor for oxidized LDL (LOX-1) by oxidized LDL and implications in **apoptosis** of human coronary artery endothelial cells: evidence from use of **antisense** LOX-1 mRNA and chemical inhibitors.
Li D; Mehta JL
Department of Medicine, University of Florida, Gainesville 32610, USA.

Arteriosclerosis, thrombosis, and vascular biology (UNITED STATES) Apr 2000, 20 (4) p1116-22, ISSN 1079-5642 Journal Code: B89
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

A specific lectin-like endothelial receptor for oxidized low density **lipoprotein** (LOX-1), distinct from the scavenger receptor in monocytes/macrophages, has been identified and cloned. In this study, we examined the regulation of LOX-1 by oxidized low density **lipoprotein** (ox-LDL) and determined the role of LOX-1 in ox-LDL-induced **apoptosis** of cultured human coronary artery endothelial cells (HCAECs). Incubation of HCAECs with ox-LDL (40 microg/mL), but not native LDL, for 24 hours markedly increased LOX-1 expression (mRNA and protein). After 48 hours of preincubation of HCAECs with a specific **antisense** to LOX-1 mRNA (**antisense** LOX-1), ox-LDL-mediated upregulation of LOX-1 was suppressed ($P<0.01$). In contrast, treatment of HCAECs with sense LOX-1 had no effect. Ox-LDL also induced **apoptosis** (determined by terminal deoxynucleotidyl transferase-mediated dUTP nick end-labeling and DNA laddering) of HCAECs in a concentration- and time-dependent fashion. LOX-1 played an important role in ox-LDL-mediated **apoptosis** of HCAECs because **antisense** LOX-1 inhibited this effect of ox-LDL. Polyinosinic acid and carrageenan, 2 different chemical inhibitors of LOX-1, also decreased ox-LDL-mediated **apoptosis** of HCAECs. Nuclear factor (NF)-kappaB was markedly activated in ox-LDL-treated HCAECs. The critical role of NF-kappaB activation became evident in experiments with **antisense** LOX-1, which abolished ox-LDL-mediated NF-kappaB activation. In this process, an NF-kappaB inhibitor, caffeic acid phenethyl ester, also inhibited ox-LDL-mediated **apoptosis** of HCAECs. These findings indicate that ox-LDL upregulates its own endothelial receptor. Ox-LDL-induced **apoptosis** is mediated by the action of LOX-1. In this process, NF-kappaB activation may play an important role as a signal transduction mechanism.

9/3,AB/20 (Item 20 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10268876 99410823 PMID: 10479664

Efficient nuclear delivery of **antisense** oligodeoxynucleotides and selective inhibition of CETP expression by **apo** E peptide in a human CETP-stably transfected CHO cell line.

Liu K; Ou J; Saku K; Jimi S; Via DP; Sparrow JT; Zhang B; Pownall HJ; Smith LC; Arakawa K
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Arteriosclerosis, thrombosis, and vascular biology (UNITED STATES) Sep 1999, 19 (9) p2207-13, ISSN 1079-5642 Journal Code: B89
Contract/Grant No.: HL056865, HL, NHLBI; HL30914, HL, NHLBI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

N,N-Dipalmitylglycyl-**apolipoprotein** E (129-169) peptide (dpGapoE) is an efficient gene delivery system for both plasmids and **antisense** oligodeoxynucleotides (ODNs). To develop a new and efficient approach to the regulation of cholesteryl ester transfer protein (CETP) expression, we used dpGapoE to transfect phosphorothioate **antisense** ODNs against nucleotides 329 to 349 of human CETP cDNA into a human CETP-stably transfected Chinese hamster ovary (CHO) cell line (hCETP-CHO). After transfection, translocation to the nuclei and concentration in nuclear structures were observed in >95% of the cells at 6 and 12 hours by fluorescence microscopy. No membrane disruption was observed after transfection of ODNs by dpGapoE. Although the translocation stability of phosphorothioate ODNs in the nuclei continued for >48 hours, it had weakened after 24 hours. Cellular CETP mRNA levels gradually declined, and

the maximum reduction in the mRNA level (>50%) was observed at 36 hours, after which the mRNA level started to recover. CETP activity in the culture medium declined over 72 hours. The maximum reduction in CETP activity was observed at 36 hours (53.8% of control). Neither CETP mRNA nor CETP activities changed throughout the experiment after the transfection of sense phosphorothioate ODNs delivered by dpGapoE complex or naked **antisense** ODNs. We conclude that (1) the novel synthetic dpGapoE was a highly effective and nontoxic vehicle for the nuclear delivery of **antisense** ODNs into hCETP-CHO cells and (2) **antisense** ODNs selectively inhibited both CETP expression and activity in an hCETP-CHO cell line. This approach may enable gene regulation in vivo and could possibly be used as an antiatherosclerotic agent to alter high density **lipoprotein** metabolism.

9/3,AB/21 (Item 21 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10201778 99332721 PMID: 10404642
Low density **lipoprotein**-receptor plays a major role in the binding of very low density **lipoproteins** and their remnants on HepG2 cells.
Truong TQ; Falstrault L; Tremblay C; Brissette L
Departement des Sciences Biologiques, Universite du Quebec a Montreal, Canada.
international journal of biochemistry & cell biology (ENGLAND) Jun 1999, 31 (6) p695-705, ISSN 1357-2725 Journal Code: CDK
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The binding to HepG2 cells of very low density **lipoproteins** (VLDL) and their remnants (IDL) was alternatively, in the past, attributed to the low density **lipoprotein** receptor (LDLr) or to an **apoE**-specific receptor. In order to resolve this issue, we have compared the binding of those **lipoproteins** labelled with iodine-125 to normal and LDLr deficient HepG2 cells. Those deficient cells were obtained by a constitutive **antisense** strategy and their LDLr level is 14% the level of normal HepG2 cells. By saturation curve analysis, we show that VLDL and IDL bind to high and low affinity sites on cells. The low affinity binding was eliminated by conducting the assay in presence of a 200-fold excess of HDL3 respective to the concentrations of 125I-labelled VLDL and IDL. For 125I-VLDL high affinity binding to normal HepG2 cells, we found a dissociation constant (Kd) of 21.2 +/- 3.7 micrograms prot./ml (S.E., N = 5) and a maximal binding capacity (Bmax) of 0.0312 +/- 0.0063 microgram prot./mg cell prot, while we have measured a Kd of 5.3 +/- 0.8 and a Bmax of 0.0081 +/- 0.0014 with LDLr deficient cells. This indicates that LDLr is responsible for 74% of VLDL binding to HepG2 cells and that the non-LDLr high affinity receptor has a higher affinity for VLDL than LDLr. A 53% loss of 125I-IDL binding capacity was measured with LDLr deficient cells compared with normal cells (Bmax: 0.028 +/- 0.005 versus 0.059 +/- 0.006), while no significant statistical difference was found between affinities. The study shows that the LDLr is almost the only contributor in VLDL binding, while it shares IDL binding capacity with another high affinity receptor. The physiological importance of LDLr is confirmed by an almost equivalent loss of IDL and VLDL degradation in LDLr deficient cells.

9/3,AB/22 (Item 22 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10070823 99164115 PMID: 10064615
Bcl-2 alters the balance between **apoptosis** and necrosis, but does not prevent cell death induced by oxidized low density **lipoproteins**.
Meilhac O; Escargueil-Blanc I; Thiers JC; Salvayre R; Negre-Salvayre A
INSERM U-466 and Department of Biochemistry and Molecular Biology,

IFR-31, CHU Rangueil, Toulouse, France.
FASEB journal (UNITED STATES) Mar 1999, 13 (3) p485-94, ISSN 0892-6638 Journal Code: FAS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Oxidized low density **lipoproteins** (oxLDL) participate in atherosclerosis plaque formation, rupture, and subsequent thrombosis. Because oxLDL are toxic to cultured cells and Bcl-2 protein prevents **apoptosis** , the present work aimed to study whether Bcl-2 may counterbalance the toxicity of oxLDL. Two experimental model systems were used in which Bcl-2 levels were modulated: 1) lymphocytes in which the (high) basal level of Bcl-2 was reduced by **antisense** oligonucleotides; 2) HL60 and HL60/B (transduced by Bcl-2) expressing low and high Bcl-2 levels, respectively. In cells expressing relatively high Bcl-2 levels (lymphocytes and HL60/B), oxLDL induced mainly primary necrosis. In cells expressing low Bcl-2 levels (**antisense**-treated lymphocytes, HL60 and ECV-304 endothelial cells), the rate of oxLDL-induced **apoptosis** was higher than that of primary necrosis. OxLDL evoked a sustained calcium rise, which is a common trigger to necrosis and **apoptosis** since both types of cell death were blocked by the calcium chelator EGTA. Conversely, a sustained calcium influx elicited by the calcium ionophore A23187 induced necrosis in cells expressing high Bcl-2 levels and **apoptosis** in cells expressing low Bcl-2 levels. This suggests that Bcl-2 acts downstream from the calcium peak and inhibits only the **apoptotic** pathway, not the necrosis pathway, thus explaining the apparent shift from oxLDL-induced **apoptosis** toward necrosis when Bcl-2 is overexpressed.

9/3,AB/23 (Item 23 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10069934 99174118 PMID: 10073970
Upregulation of superoxide dismutase and nitric oxide synthase mediates the **apoptosis** -suppressive effects of shear stress on endothelial cells.
Dimmeler S; Hermann C; Galle J; Zeiher AM
Department of Internal Medicine IV, Division of Cardiology, University of Frankfurt, Germany.
Arteriosclerosis, thrombosis, and vascular biology (UNITED STATES) Mar 1999, 19 (3) p656-64, ISSN 1079-5642 Journal Code: B89
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Physiological levels of laminar shear stress completely abrogate **apoptosis** of human endothelial cells in response to a variety of stimuli and might therefore importantly contribute to endothelial integrity. We show here that the **apoptosis**-suppressive effects of shear stress are mediated by upregulation of Cu/Zn SOD and NO synthase. Shear stress-mediated inhibition of endothelial cell **apoptosis** in response to exogenous oxygen radicals, oxidized LDL, and tumor necrosis factor-alpha was associated with complete inhibition of caspase-3-like activity, the central effector arm executing the **apoptotic** cell death program in endothelial cells. Shear stress-dependent upregulation of Cu/Zn SOD and NO synthase blocks activation of the caspase cascade in response to **apoptosis**-inducing stimuli. These findings establish the upregulation of Cu/Zn SOD and NO synthase by shear stress as a central protective cellular mechanism to preserve the integrity of the endothelium after proapoptotic stimulation.

9/3,AB/24 (Item 24 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09756082 98215233 PMID: 9555948
Chylomicron remnant uptake is regulated by the expression and function of heparan sulfate proteoglycan in hepatocytes.
Zeng BJ; Mortimer BC; Martins IJ; Seydel U; Redgrave TG
Department of Physiology, The University of Western Australia, Nedlands.
Journal of lipid research (UNITED STATES) Apr 1998, 39 (4) p845-60, ISSN 0022-2275 Journal Code: IX3
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Chylomicron remnants transport cholesterol from the intestine, and are removed from the circulation principally by the liver. While hepatic receptors, including the low density **lipoprotein** (LDL) receptor account for endocytosis, heparan sulfate proteoglycans (HSPG) participate in the initial binding of remnants to liver cells. To explore the interactions between HSPG and endocytosis of remnants, in the present study the expression of HSPG was inhibited in HepG2 cells transfected by a synthetic **antisense** oligodeoxynucleotide SYN5. Immunofluorescent staining by a monoclonal anti-syndecan antibody showed significant reduction in the expression of syndecan in SYN5-treated cells compared with control cells. Remnant binding decreased by about 50-70% in SYN5-transfected cells. Monoclonal antibodies to either heparan sulphate or the LDL receptor decreased binding by about 60-65%. The glycosylation inhibitor beta-nitrophenylxylopyranoside inhibited remnant uptake by 25%, whereas 4-nitrophenyl-beta-D-galactopyranoside had no effect on remnant binding. Heparinase completely abolished binding at appropriate concentrations. Heparitinase was less effective than hep arinase in inhibiting remnant binding. Suramin completely abolished the remnant binding. Poly-arginine, poly-lysine, and protamine all reduced remnant uptake by the cells, as did polybrene, a synthetic polycation, suggesting a role of cation-anion interactions in remnant binding. Brefeldin A, colchicine, and monensin caused the fluorescence associated with remnants to persist within the cells, confirming that blockers of tubulovesicular processes and Golgi function inhibit the intracellular transport and degradation of the remnants. Our results show that remnant binding to liver cells depends on the LDL receptor, on the expression of HSPG core proteins, and on the functionality of heparan sulfate in HSPG.

9/3,AB/25 (Item 25 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09706618 98194866 PMID: 9535218
Apoptosis caused by oxidized LDL is manganese superoxide dismutase and p53 dependent.
Kinscherf R; Claus R; Wagner M; Gehrke C; Kamencic H; Hou D; Nauen O; Schmiedt W; Kovacs G; Pill J; Metz J; Deigner HP
Department of Anatomy and Cell Biology III, University of Heidelberg, Germany.
FASEB journal (UNITED STATES) Apr 1998, 12 (6) p461-7, ISSN 0892-6638 Journal Code: FAS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Oxidized low density **lipoprotein** (oxLDL) induces **apoptosis** in human macrophages (Mphi), a significant feature in atherogenesis. We found that induction of **apoptosis** in Mphi by oxLDL, C2-ceramide, tumor necrosis factor alpha (TNF-alpha), and hydrogen peroxide (H2O2) was associated with enhanced expression of manganese superoxide dismutase (MnSOD) and p53. Treatment of cells with p53 or MnSOD **antisense** oligonucleotides prior to stimulation with oxLDL, C2-ceramide, TNF-alpha, or H2O2 caused an inhibition of the expression of the respective protein together with a marked reduction of **apoptosis** . Exposure to

N-acetylcysteine before treatment with oxLDL, C2-ceramide, TNF-alpha, or H2O2 reversed a decrease in cellular glutathione concentrations as well as the enhanced production of p53 and MnSOD mRNA and protein. In **apoptotic** macrophages of human atherosclerotic plaques, colocalization of MnSOD and p53 immunoreactivity was found. These results indicate that in oxLDL-induced **apoptosis**, a concomitant induction of p53 and MnSOD is critical, and suggest that it is at least in part due to an enhancement of the sphingomyelin/ceramide pathway.

9/3,AB/26 (Item 26 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09642713 98070210 PMID: 9405278
Effect of reduced low-density **lipoprotein** receptor level on HepG2 cell cholesterol metabolism.
Izem L; Rassart E; Kamate L; Falstrault L; Rhainds D; Brissette L
Departement des Sciences Biologiques, Universite du Quebec a Montreal, C.P. 8888, Succ. Centre-ville, Montreal, Quebec, Canada H3C 3P8.
Biochemical journal (ENGLAND) Jan 1 1998, 329 (Pt 1) p81-9, ISSN 0264-6021 Journal Code: 9YO
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Low-density **lipoproteins** (LDL) are taken up by both LDL receptor (LDLr)-dependent and -independent pathways. In order to determine the importance of these pathways in the activity of the various enzymes that are important in maintaining the cellular cholesterol level in hepatic cells, we created HepG2 cells expressing lower levels of LDLr. Thus HepG2 cells were transfected with a constitutive expression vector (pRc/CMV) containing a fragment of LDLr cDNA inserted in an **antisense** manner. Stable transformants were obtained that showed significant reductions of 42, 72 and 85% of LDLr protein levels compared with the control, as demonstrated by immunoblotting and confirmed by the LDL binding assay. The best inactivation was achieved with the construct containing the first 0.7 kb of LDLr cDNA. Incubating the different HepG2 cell subtypes with LDL showed similar association of **apolipoprotein** B (**apo** B) or cholesteryl esters from LDL with the cells, indicating that the LDLr deficiency did not significantly affect LDL uptake by the cell. However, **apoB** degradation was reduced significantly by 71-82% in the most LDLr-deficient HepG2 cells. We also found that 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCoA red) activity is significantly increased by 32-35% in HepG2 cells expressing very low levels of LDLr that also demonstrate a significant decrease of 20% in acyl-CoA:cholesterol acyltransferase (ACAT) activity. However, these effects are moderate compared with those observed when cells were incubated in **lipoprotein**-depleted medium, where a >900% increase in HMGCoA red activity and a loss of 60% of ACAT activity was observed. Thus, in HepG2 cells, different levels of LDLr affect LDL-**apoB** degradation, but have very little effect on LDL association, HMGCoA red and ACAT activities, revealing that LDLr is more important in the clearance of LDL-**apoB** than in HepG2 cell cholesterol homoeostasis, a role that should be attributable to both LDLr-dependent and -independent pathways.

9/3,AB/27 (Item 27 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09529370 97277947 PMID: 9131298
Use of gene-manipulated models to study the physiology of lipid transport.
Mortimer BC; Martins I; Zeng BJ; Redgrave TG
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Clinical and experimental pharmacology & physiology (AUSTRALIA) Mar-Apr 1997, 24 (3-4) p281-5, ISSN 0305-1870 Journal Code: DD8

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

1. In vivo and in vitro gene-manipulated models were used to study the metabolism of chylomicron remnants. Transgenic mice expressing human **apolipoprotein** (**Apo**) A1 or E4, gene knockout mice deficient in **ApoE** or low density **lipoprotein** (LDL) receptors and **antisense** gene inhibition in HepG2 cells were used to evaluate the effect of gene manipulations on the metabolism of chylomicron remnants. 2. Mice transgenic for human **ApoE4** showed accelerated clearance of chylomicron-like emulsions when animals were fed a low-fat diet. When challenged by a high-fat diet, remnant clearance in **ApoE4** transgenic mice was delayed, as in normal or non-transgenic controls. However, unlike normal nontransgenic controls, in **ApoE4** transgenic mice high density **lipoprotein** (HDL)-cholesterol levels remained high after high-fat feeding, which probably protected the animals from the development of atherosclerosis. In contrast, clearance of chylomicron-like lipid emulsions was not affected by the over-expression of human **ApoAI** in transgenic mice. 3. Gene knock-out mice deficient in **ApoE** or deficient in the LDL receptor were used to show that **ApoE** and LDL receptors are both essential for the normal, fast catabolism of chylomicron remnants by the liver. In the absence of the LDL receptor, an alternative **ApoE** -dependent pathway operates to clear chylomicrons from the plasma, with significantly delayed catabolism. 4. **Antisense** gene inhibition techniques were used to suppress the expression of syndecan, a core protein of heparan sulfate proteoglycan, in HepG2 cells. Remnant uptake in cells transfected with the **antisense** oligodeoxynucleotide complementary to a 20 nucleotide sequence upstream of the initiation site of syndecan cDNA markedly reduced the uptake of chylomicron remnant.

9/3,AB/28 (Item 28 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08955218 96325006 PMID: 8702580

Changes in plasma **lipoprotein** cholesterol levels by **antisense** oligodeoxynucleotides against cholesteryl ester transfer protein in cholesterol-fed rabbits.

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Journal of biological chemistry (UNITED STATES) Aug 9 1996, 271 (32) p19080-3, ISSN 0021-9258 Journal Code: HIV

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

Cholesteryl ester transfer protein (CETP) is the enzyme that facilitates the transfer of cholesteryl ester from high density **lipoprotein** (HDL) to **apoB**-containing **lipoproteins** and also affects the low density **lipoprotein** metabolism. On the other hand, the liver is the major tissue responsible for the production of CETP (CETP mRNA) in rabbits. To test the hypothesis that a reduction of CETP mRNA in the liver by **antisense** oligodeoxynucleotides (ODNs) may affect the plasma **lipoprotein** cholesterol levels, we intravenously injected **antisense** ODNs against rabbit CETP coupled with asialoglycoprotein carrier molecules, which serve as an important method to regulate liver gene expression, to cholesterol-fed rabbits via their ear veins. All rabbits were fed a standard rabbit chow supplement with 0.1% cholesterol for 10 weeks before and throughout the experiment. After injecting rabbits with **antisense** ODNs, the plasma total cholesterol concentrations and plasma CETP activities all decreased at 24, 48, and 96 h, whereas the plasma HDL cholesterol concentrations increased at 48 h. A reduction in the

hepatic CETP mRNA was also observed at 6, 24, and 48 h after the injection with **antisense** ODNs. However, in the rabbits injected with sense ODNs, the plasma total and HDL cholesterol concentrations and the plasma CETP activities did not significantly change, and the hepatic CETP mRNA did not change either throughout the experimental period. Although the exact role of CETP in the development of atherosclerosis remains to be clarified, these findings showed for the first time that the intravenous injection with **antisense** ODNs against CETP coupled to asialoglycoprotein carrier molecules targeted to the liver could thus inhibit plasma CETP activity and, as a result, could induce a decrease in the plasma low density **lipoprotein** and very low density **lipoprotein** cholesterol and an increase in the plasma HDL cholesterol in cholesterol-fed rabbits.

9/3,AB/29 (Item 29 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08811868 96371109 PMID: 8774944
Expression and distribution of low density **lipoprotein** receptor-related protein mRNA in the rat central nervous system.
Ishiguro M; Imai Y; Kohsaka S
Department of Neurochemistry, National Institute of Neuroscience, Tokyo, Japan.
Brain research. Molecular brain research (NETHERLANDS) Oct 1995, 33 (1) p37-46, ISSN 0169-328X Journal Code: MBR
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The low density **lipoprotein** receptor-related protein (LRP) is a multifunctional cell surface receptor that binds to the protease inhibitor alpha 2-macroglobulin (alpha 2 M). LRP has also been identified as the **apolipoprotein** E (**apoE**) receptor that mediates lipid metabolism. Recently it has been reported that **apoE4**, one of three common isoforms of **apoE**, is a main risk factor of Alzheimer's disease (AD). Moreover, all three of these proteins are reported to accumulate in the senile plaques in the brains of Alzheimer's patients. To understand the roles of LRP in the normal development of the central nervous system (CNS) and in the pathogenesis of AD, we studied the developmental expression and localization of LRP mRNA in the CNS. We used Northern blot analysis to investigate the developmental profile of LRP mRNA in the rat brain. LRP mRNA was first detected as early as in 18-day-old embryonic rat brain and was continuously expressed thereafter. A particularly high level of expression of the mRNA was observed in the perinatal stage. We also determined the cellular distribution of LRP mRNA in the CNS of 20-day-old embryonic and 6-week-old adult rat brains by in situ hybridization using a digoxigenin-labeled **antisense** riboprobe to LRP mRNA. In the embryonic rat brain, LRP mRNA was highly expressed in most of the cells, mainly neurons and glial cells. In the adult rat, LRP mRNA was expressed mostly in neurons in both the brain and the spinal cord. These results suggest that LRP plays crucial roles in development of the brain.

9/3,AB/30 (Item 30 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08487911 95221379 PMID: 7706266
Studies on the translocation of the amino terminus of **apolipoprotein** B into the endoplasmic reticulum.
Pease RJ; Leiper JM; Harrison GB; Scott J
Medical Research Council Molecular Medicine Group, Royal Postgraduate Medical School, London, United Kingdom.
Journal of biological chemistry (UNITED STATES) Mar 31 1995, 270 (13) p7261-71, ISSN 0021-9258 Journal Code: HIV

Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Apolipoprotein (**apo**) B is either co-translationally assembled into **lipoproteins** , or becomes associated with the membrane of the endoplasmic reticulum (ER) and is subsequently degraded. It has been proposed that **apoB** undergoes a novel process of translocation which generates cytoplasmically exposed **apoB** in the ER of hepatic and non-hepatic cells. Transmembrane forms of **apoB** can also be generated by in vitro translation (Chuck, S. L., and Lingappa, V. R. (1992) Cell 68, 9-21), which might explain the origin of untranslocated **apoB** in vivo. Here we have investigated a protocol which generates transmembrane forms of **apoB** during in vitro translation of truncated RNA transcripts. We observe that **apoB** can become transmembrane at sites of ribosome pausing and be held in this configuration by persistence of tRNA on the peptide chains. Ribosome pausing also occurs at these same sites in the absence of acceptor microsomes. Transmembrane topology can be generated at sites of ribosome pausing in a cytosolic protein, sea urchin cyclin when fused to a signal sequence. Mapping of the ribosome pause sites in **apoB** and in cyclin revealed no amino acid sequence homology. Chimeric constructs with engineered downstream glycosylation sites showed no evidence that ribosome pause sequences affect translocation of transcripts with termination codons. Transmembrane forms of **apoB** and cyclin were not generated during translocation into the ER in transfected COS cells.

9/3,AB/31 (Item 31 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08111461 94137695 PMID: 8305414

Overexpression of human **lipoprotein** lipase enhances uptake of **lipoproteins** containing **apolipoprotein** B-100 in transfected cells.

Kawamura M; Shimano H; Gotoda T; Harada K; Shimada M; Ohsuga J; Inaba T; Watanabe Y; Yamamoto K; Kozaki K; et al
Third Department of Internal Medicine, University of Tokyo, Japan.
Arteriosclerosis and thrombosis (UNITED STATES) Feb 1994, 14 (2) p235-42, ISSN 1049-8834 Journal Code: AZ1
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

To investigate the role in **lipoprotein** metabolism of **lipoprotein** lipase (LPL) secreted by tissues, we established two cell lines. Fusion plasmids containing either human LPL cDNA or **antisense** LPL cDNA under control of the cytomegalovirus promoter were transfected into Chinese hamster ovary (CHO) cells, designated as CHO-LPL and CHO-anti-LPL, respectively. CHO-LPL constitutively produced a high level of LPL, whereas CHO-anti-LPL produced a minimal level. When very-low-density **lipoprotein** (VLDL) was incubated with CHO-LPL, VLDL triglycerides were hydrolyzed, intermediate-density **lipoprotein** (IDL) was produced, and **apolipoprotein** E contents increased. CHO-LPL took up and degraded 125I-VLDL at 37 degrees C four times more strongly than did CHO-anti-LPL. Whereas the degradation of **apolipoprotein** E-deficient VLDL was only 12% that of normal VLDL in CHO-LPL, structural changes of the **lipoprotein**, including **apolipoprotein** E expression on the **lipoprotein** surface, may be important for the cellular uptake of VLDL. Furthermore, we found that binding at 4 degrees C of VLDL and LDL to CHO-LPL was greater than to CHO-anti-LPL, and this binding difference was abolished by washing the cells with heparin. This suggests that cell surface LPL plays a role in the binding of **lipoproteins** to the cells. We conclude that both the composition of VLDL particles and their cellular binding are influenced by LPL secreted by cells, both of which may enhance the cellular uptake of VLDL.

9/3,AB/32 (Item 32 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07713432 93016049 PMID: 1328226
Regulated expression of the trophoblast alpha 2-macroglobulin receptor/low density **lipoprotein** receptor-related protein. Differentiation and cAMP modulate protein and mRNA levels.
Gafvels ME; Coukos G; Sayegh R; Coutifaris C; Strickland DK; Strauss JF
Department of Obstetrics and Gynecology, University of Pennsylvania School of Medicine, Philadelphia 19104.
Journal of biological chemistry (UNITED STATES) Oct 15 1992, 267 (29) p21230-4, ISSN 0021-9258 Journal Code: HIV
Contract/Grant No.: GM-42581, GM, NIGMS; HD-06274, HD, NICHD; HD-29946, HD, NICHD
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The alpha 2-macroglobulin receptor/low density **lipoprotein** receptor-related protein (alpha 2MR/LRP) has several ligands including activated alpha 2-macroglobulin, pregnancy zone protein, and very low density **lipoproteins** enriched with **apolipoprotein** E. The diversity of ligands suggests a role for the alpha 2MR/LRP in a variety of processes including tissue remodeling and **lipoprotein** metabolism. We examined alpha 2MR/LRP in placental trophoblasts, invasive cells that also function in lipid transport and cholesterol metabolism. alpha 2MR/LRP protein was localized by immunohistochemistry in the syncytiotrophoblast of term placenta. Cytotrophoblasts did not stain prominently. alpha 2MR/LRP (protein and message) in primary cultures of human trophoblast cells increased as cytotrophoblasts differentiated into syncytiotrophoblast. 8-Bromo-cAMP prevented this increase and suppressed alpha 2MR/LRP expression. The cyclic nucleotide had similar suppressive effects on alpha 2MR/LRP in BeWo choriocarcinoma cells. In contrast, low density **lipoprotein** receptor gene expression was increased. We conclude that: 1) there is a differentiation-dependent pattern of alpha 2MR/LRP expression in the human trophoblast; 2) cAMP negatively regulates alpha 2MR/LRP; 3) there is an inverse relationship between alpha 2MR/LRP and low density **lipoprotein** receptor gene expression in trophoblast cells.

9/3,AB/33 (Item 33 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05925807 89071788 PMID: 2462254
Localization of mRNA for low density **lipoprotein** receptor and a cholesterol synthetic enzyme in rabbit nervous system by in situ hybridization.
Swanson LW; Simmons DM; Hofmann SL; Goldstein JL; Brown MS
Salk Institute for Biological Studies, La Jolla, CA 92037.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Dec 1988, 85 (24) p9821-5, ISSN 0027-8424 Journal Code: PV3
Contract/Grant No.: HL20948, HL, NHLBI; NS16686, NS, NINDS
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The low density **lipoprotein** receptor and one of its ligands, **apoprotein** E, are known to be synthesized in the central nervous system. In the current study, we used in situ hybridization to localize the receptor mRNA in selected neurons and glia throughout the nervous system of 9-day-old rabbits. Particularly high levels were found in sensory ganglia, sensory nuclei, and motor-related nuclei. The same regions contained high levels of mRNA for 3-hydroxy-3-methylglutaryl-coenzyme A synthase, a regulated enzyme in cholesterol biosynthesis. The distribution of low

density **lipoprotein** receptor mRNA was similar in mature and immature rabbits. The data suggest that certain cells in the nervous system have high requirements for cholesterol, which they satisfy through cholesterol synthesis and through receptor-mediated uptake of cholesterol-carrying **lipoproteins**. The latter originate in astrocytes which synthesize and secrete **apoprotein** E. These data suggest that the nervous system of mammals contains an active system for continuous redistribution and recycling of cholesterol that is physically distinct from the **lipoprotein** transport system in plasma.

9/3,AB/34 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13050430 BIOSIS NO.: 200100257579
Tissue factor and tissue factor pathway inhibitor mRNA expression in the lung and kidney of LDL receptor deficient and **Apo**-E deficient mice.
AUTHOR: Minchenko Alexander G(a); Opentanova Irina L(a); Lanza-Jacoby Susan (a); Armstead Valerie E(a)
AUTHOR ADDRESS: (a)Jefferson Med. College, Thomas Jefferson Univ., 1020 Locust St., 408E JAH, Philadelphia, PA, 19107**USA
JOURNAL: FASEB Journal 15 (4):pA102 March 7, 2001
MEDIUM: print
CONFERENCE/MEETING: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Tissue factor (TF) is a transmembrane glycoprotein responsible for initiating the extrinsic pathway of coagulation in normal hemostasis and in atherosclerotic diseases. Tissue factor pathway inhibitor (TFP1) is a potent inhibitor of TF-induced coagulation and may play a role in regulating coagulation in atherosclerotic plaque. In the present study, we investigated TF and TFPI mRNA expression in the lung and kidney of genetically modified hyperlipidemic mice compared to wild-type (C57BL6) mice. Radiolabeled **antisense** RNA probes were used to study TF and TFPI mRNA expression. 18S ribosomal RNA was employed to control for ubiquitous RNA. The study revealed that TF mRNA expression significantly increased in the lung (+50%; P < 0.05) but slightly decreased in the kidney (-24%; P < 0.05) of **Apo**-E -/- mice. The changes in TF mRNA expression were accompanied by correlative changes in TFPI mRNA expression in the lung and kidney of **Apo**-E -/- mice. However, TF mRNA expression in the lung of LDL receptor -/- mice decreased (-28%; P < 0.05) while TFPI mRNA levels were increased (+57%; P < 0.01). TFPI mRNA expression in the kidney of LDL receptor -/- mice decreased (-39 %; P < 0.05) although TF mRNA expression did not change significantly. These results indicate TF and TFPI mRNA expression is altered compared to the wild-type mouse in the lung and kidney of hyperlipidemic **Apo**-E and LDL receptor -/- mice by different mechanisms. The absence of **Apo**-E in **Apo**-E -/- mice but not in LDL receptor -/- mice may explain these differences between the two mouse strains.

2001

9/3,AB/35 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12213503 BIOSIS NO.: 199900508352

Apolipoprotein B mRNA specific hammerhead **ribozyme** reduces **apolipoprotein** B and plasma cholesterol levels in mice.
AUTHOR: Enjoji Munechika; Tsai An; Kobayashi Kunihisa; Chen Lawrence; Teng Ba-Bie
AUTHOR ADDRESS: Baylor Coll. Med., Houston, TX**USA
JOURNAL: Circulation 98 (17 SUPPL.):pI2-I3 Oct. 27, 1998
CONFERENCE/MEETING: 71st Scientific Sessions of the American Heart Association Dallas, Texas, USA November 8-11, 1998
SPONSOR: The American Heart Association
ISSN: 0009-7322
RECORD TYPE: Citation
LANGUAGE: English
1998

9/3,AB/36 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09566958 BIOSIS NO.: 199598021876
Apolipoprotein E-deficient mice created by systemic **antisense** oligonucleotides administration: A new model for **lipoprotein** metabolism studies.
AUTHOR: Morishita Ryuichi(a); Gibbons Gary H(a); Tomita Naruya(a); Zhang Lunan(a); Kaneda Yasufumi; Ogihara Toshio; Dzau Victor J(a)
AUTHOR ADDRESS: (a)Div. Cardiovascular Med., Falk Cardiovascular Res. Cent., Stanford Univ., Stanford, CA**USA
JOURNAL: Circulation 90 (4 PART 2):pI134 1994
CONFERENCE/MEETING: 67th Scientific Sessions of the American Heart Association Dallas, Texas, USA November 14-17, 1994
ISSN: 0009-7322
RECORD TYPE: Citation
LANGUAGE: English
1994

9/3,AB/37 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09296741 BIOSIS NO.: 199497305111
Apolipoprotein E-deficient mice created by systemic administration of **antisense** oligonucleotides: A new model for **lipoprotein** metabolism studies.
AUTHOR: Morishita R; Gibbons G H; Nakajima M; Zhang L; Kaneda Y; Ogihara T; Dzau V J
AUTHOR ADDRESS: Div. Cardiovascular Med., Falk Cardiovascular Research Center, Stanford Univ., Stanford, CA**USA
JOURNAL: Clinical Research 42 (2):p176A 1994
CONFERENCE/MEETING: Meeting of the American Federation for Clinical Research Baltimore, Maryland, USA April 29-May 2, 1994
ISSN: 0009-9279
RECORD TYPE: Citation
LANGUAGE: English
1994

9/3,AB/38 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07319100 BIOSIS NO.: 000090099000
THE TRANSGENIC RABBITS CONTAINING A HUMAN **APO LIPOPROTEIN** A-I **ANTISENSE** GENE AS A MODEL FOR THE GENETIC CORRECTION OF ATHEROGENIC

DISTURBANCES OF LIPID METABOLISM

AUTHOR: PEREVOZCHIKOV A P; VAISMAN B L; DOZORTSEV D I; SOROKIN A V; ORLOV S V; DENISENKO A D; DYBAN A P; KLIMOV A N
AUTHOR ADDRESS: RES. INST. EXP. MED., ACAD. MED. SCI. USSR, LENINGRAD, USSR.

JOURNAL: BIOPOLIM KLETKA 6 (2). 1990. 17-24. 1990
FULL JOURNAL NAME: Biopolimery i Kletka
CODEN: BIKLE
RECORD TYPE: Abstract
LANGUAGE: RUSSIAN

ABSTRACT: The recombinant DNA molecules containing potentially expressing human **apoA**-I **antisense** gene were constructed and injected into the rabbit zygotes. Dot-blot hybridization techniques as well as lipid and **lipoprotein** analyses methods were used to reveal transgenic animals. It was found that DNAs of several rabbits contained up to 40 copies of molecules of foreign DNA per genome. It was interesting that the patterns of serum lipid and **lipoprotein** metabolism of transgenic animals were shifted to atherogenic phenotype. In one case the expression of the **antisense** gene was able to suppress the synthesis of high-density **lipoproteins**. In two other cases the expression of this gene as appeared was correlated with a decrease of .alpha.-**lipoprotein** cholesterol level. In all the cases serum cholesterol and (or) triglyceride levels increased as well. Thus, the obtained transgenic rabbits may serve as a model to study and genetically correct atherogenic disturbances of lipid metabolism.

1990